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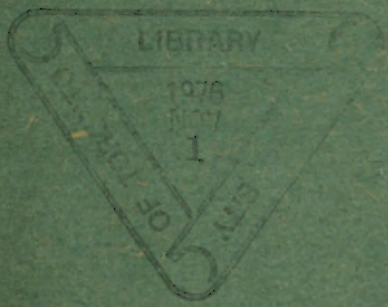


LONDON:
SOCIETY OF TROPICAL MEDICINE AND HYGIENE
11 CHANDOS STREET, CAVENDISH SQUARE, W.

## DEMONSTRATION BY THE PRESIDENT OF A CASE OF KALA AZAR, APPARENTLY CURED.

(*Friday, March* 19, 1909.)

Sir Patrick Manson said he wished to show the Fellows a case — the second within six months — of recovery, or apparent recovery, from kala azar. The first case was a missionary who had contracted the disease abroad, and who, after prolonged treatment by atoxyl, had completely regained his health. The patient present to-night had been for twelve years an officer in the Indian army, and during that time had been stationed on the North-West Frontier, in Southern India, Burma, and elsewhere. With one or two exceptions, until his present illness began he had enjoyed good health. In 1900 he had had an attack of malaria, and a recurrence of that disease, apparently, in 1904, but, until September 12, 1907, he was quite well. He was then seized with a severe fever which was diagnosed as typhoid. After this illness, which lasted about two months, he went to Ceylon for a change; there he was seen by Dr. Castellani, who examined his blood during a recurrence of fever, with the result that the malignant tertian malarial parasite was found. He was dosed liberally with quinine and went again to Burma. On his return, there was a relapse in Rangoon; and from that time until he (Sir Patrick Manson) saw him in April 1908, the patient suffered, practically all the time, from continued fever. In addition to the fever he had several other complications, such as subacute synovitis, sciatica, orchitis, and thrombosis of

the veins of the left leg. From these he made a good recovery. He then presented all the clinical phenomena of typical kala azar — an enormously enlarged spleen, down to the level of the umbilicus, a greatly enlarged liver, quite a hand's breadth or more, reaching almost to the level of the umbilicus, with emaciation and anæmia. He (Sir Patrick Manson) thought he was justified in endeavouring to confirm his suspicions by puncturing the patient's liver, but first should be mentioned that when the patient was in Burma he was supposed to have had abscess of the liver, and that the liver was tapped in several places without result. He (Sir Patrick Manson) procured some liver pulp and liver blood and made a number of film preparations, which he examined microscopically. In none of these had he himself been able to find the Leishman body, but Dr. Kerr and Dr. Spitta had found in three of the slides characteristic Leishman bodies; thus the diagnosis, which had been founded on clinical phenomena, had been confirmed by microscopical investigation. The patient was put on atoxyl—3 grains every three days, or an equivalent to 1 grain per diem, and he was sent to Osborne, with directions that he should receive tonic treatment in the shape of good food, fresh air, and all the domestic comforts so liberally supplied at that institution. This treatment was faithfully carried out, apparently with but little improvement until the month of August, when the patient's general condition improved. The fever, which had been persistent, gradually and completely disappeared for the first time for many months. Since then, with one exception, the patient had been completely free from fever. His weight had increased by 22 lbs., and he felt in perfect health. More than that, the spleen, which used to extend to the umbilicus,

could now be felt with difficulty, and the liver, which had had a vertical diameter of 9 in. in the nipple line, had now a depth of about 2 in. He (Sir Patrick Manson) regarded the patient as practically cured. It could not be said that he was free from the risk of relapse, but if he remained under the same medicine and general treatment he would completely recover. The drug with which the patient was treated at first was atoxyl, but later it was thought more convenient to use soamin, and that drug—which was practically atoxyl in a purer form—was substituted. He could not positively attribute the patient's recovery to the use of atoxyl, but recovery certainly took place while using that drug. *Post hoc*, however, was not *propter hoc;* but although one or two cases did not justify a positive statement, he thought that the case of this patient encouraged them to persevere with the treatment of kala azar by atoxyl.

# OBSERVATIONS OF THE UNITED STATES ARMY BOARD FOR THE STUDY OF TROPICAL DISEASES IN THE PHILIPPINE ISLANDS UPON *FILARIA PHILIPPINENSIS*, ENTAMŒBA COLI, THE ETIOLOGY OF DENGUE, AND *TREPONEMA PERTENUIS* AND THE EXPERIMENTAL PRODUCTION OF YAWS IN MONKEYS.

By CHARLES F. CRAIG, M.D.
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This paper gives the results of research work upon tropical diseases in these Islands from March, 1906, to July, 1907. During this time the Board consisted of Captain (now Major) P. M. Ashburn, Medical Corps, and the writer, and this paper is abstracted from their reports to the Surgeon-General of the Army and their publications in the *Philippine Journal of Science*.

## I.

### *Filaria (Microfilaria philippinensis).*

That filariasis occurred in the Philippine Islands has been known since the early days of the American occupation, but it was not known that a special species of filaria was indigenous to the Islands, as all cases described previously to our work had been in the persons of foreigners, and had been diagnosed as either *F. nocturna* (*F. bancrofti*) or *diurna*. That *F. bancrofti* does occur in certain regions of the Islands has been recently demonstrated by Phelan and Nichols, who succeeded us as members of the Board, but our observations conclusively prove that a hitherto undescribed species of

filaria also occurs in the Philippines, which shows no periodicity and which is characterized by morphological features which distinguish it from the embryos of *F. bancrofti.*

In a special report submitted to the Surgeon-General of the Army in May, 1906, we described a new blood filaria of man to which the name *F. philippinensis* (sp. nov.) was given, because of its occurrence in a native of the Philippine Islands. We considered that this filaria represented a new species, and that it was probably the only one indigenous to these Islands—a new species—because of its morphology, lack of periodicity, and the rarity of filariasis in the Philippines—the only indigenous one—because the previous descriptions of the filariæ observed in natives of these Islands contained nothing which would exclude the possibility that the observers might have been dealing with *F. philippinensis.* The later researches of Phelan and Nichols, however, demonstrate that filariasis is much more common than we had supposed, and that *F. bancrofti* is the most common filaria observed. They observed one case infected with *F. philippinensis* and over a score infected with *F. bancrofti.*

Only the embryonic or micro-filarial stage of *F. philippinensis* has been observed, and in all we were able to study five instances of infection with it, one case in the person of a Visayan prisoner in Bilibid Prison, Manila, the remaining four being native soldiers, from Ambos Camarines, serving in a company of the Philippine Scouts.

*F. philippinensis* presents no periodicity, occurring in practically equal but small numbers in the peripheral blood at all hours of the day and night; it is actively motile, possessing both lashing and marked progressive

motion, and is enclosed in a tight sheath, prolonged at each extremity into a delicate whip-like lash. The worm does not move backward and forward within the sheath. The head is hemispherical in shape, and is armed with a very delicate spicule which retracts within a finely serrated prepuce; the number of lips constituting this prepuce cannot be distinguished. The sheath is only visible at the extremities of the parasite. The body presents an anterior V-spot, a central viscus, and a posterior V-spot. The central viscus is situated in the posterior portion of the central third of the body and consists of a convoluted or spiral tube, or cylinder, resembling a vine tendril, and presenting five or six spiral turns which progressively grow smaller, ending in a fine curved or straight extremity. The tail is abruptly attenuated, at a point midway between the posterior V-spot and the tip, to three-quarters of its former diameter, forming a distinct offset upon either side, while the posterior V-spot marks the site of a distinct papilla which bulges beyond the body line, and probably represents the anus or cloaca of the adult worm. The tail terminates in a very fine thread-like point. The portion of the tail beyond the attenuation is sloughed off during the development of the worm in the mosquito.

*F. philippinensis* measures on the average 0·32 mm. long by 0·0065 mm. broad, but variations occur in the length between 0·29 mm. and 0·335 mm. This micro-filaria presents no periodicity as regards the time of its appearance in the peripheral blood or the number of embryos present at any one time. We made extensive observations regarding periodicity in all five cases of infection with this micro-filaria and can state conclusively that it can be found in the peripheral blood at all hours of the day and night and in practically the same numbers

at all hours. Thus, in three of the cases, the following results were obtained, the blood examinations being made every three hours for twenty-four hours :—

Case 1.—From 7 a.m. to 7 p.m. eight filariæ were found in 13 smears. From 7 p.m. to 7 a.m. eight filariæ were found in 13 smears.

Case 2.—From 7 a.m. to 7 p.m. eight filariæ were found in 13 smears. From 7 p.m. to 7 a.m. eight filariæ were found in 13 smears.

Case 3.—From 7 a.m. to 7 p.m. eight filariæ were found in 10 smears. From 7 p.m. to 7 a.m. ten filariæ were found in 13 smears.

At no time were more than four filariæ found in a single smear, and the only times the smears were negative was once at 10 p.m. and once at 1 a.m.

The fact that this micro-filaria exhibits no periodicity and that it is a sheathed organism serves to differentiate it from any other filaria which has been described as infecting man.

As regards its pathogenicity, in none of the cases did we observe any symptoms or pathological lesions which we could feel justified in considering as due to the presence of the filaria. One patient had a history of having previously suffered from chyluria, but while under observation he presented no symptoms.

*Development in Mosquitoes.* — We made numerous examinations of mosquitoes which were infected by biting patients harbouring this filaria, most of the insects so infected being *Culex fatigans* (Wied.), some few being *Stegomyia*. No development occurred in *Stegomyia*, but in *C. fatigans* we were able to trace the complete development of *F. philippinensis* up to the time that it became lodged in the mosquito's labium and is ready to infect the next person bitten.

One of the earliest observations to be made in studying infected mosquitoes relates to the number of filariæ ingested. In some manner at present unknown the mosquito manages to obtain from the body of the patient forty to fifty times as many filariæ as it was possible for us to obtain in a similar amount of blood from a needle prick. Thus, in thick smears we usually found but one or two filariæ, and very often none. In the blood from the stomach of a mosquito which has recently bitten, the amount of blood usually appears less than is contained in the thick smears, but it was nearly always possible to find from forty to eighty filariæ. This fact appeared to us to have some practical value in the examination of cases of elephantiasis for filariæ, or in suspected cases of filariasis in which the parasites may be very few in number. By examining the blood obtained from the stomach of a mosquito allowed to bite the suspected case the chances of finding the filariæ would be greatly increased and thus the diagnosis rendered more easy.

Once in the stomach of the mosquito the filariæ continue their active motion, which is more uniformly progressive than in the blood smears, for several hours until the sheath is discarded, when the worms pierce the stomach wall and enter the body cavity, coming to rest in the thoracic muscles, where they undergo development. Briefly summarized, the history of the development of *F. philippinensis* within the mosquito, *Culex fatigans* (Wied.), is as follows: In from fourteen to fifteen days the development is complete and the filaria has passed into the labium of the mosquito; the sheath of the embryo is lost in the stomach and the worm then penetrates the stomach wall and reaches the muscles of the thorax, where most of the developmental changes occur; the filaria increases in length from 0·32 mm. to as much as

2·20 mm., and in breadth from 0·0065 mm. to 0·02 mm.; it develops a well-marked intestinal canal, divided into œsophagus and intestine, a well-defined anus and three papillæ which are situated at the end of the tail; the mouth appears to be simply a circular cavity having no distinct lips. Development, so far as the morphology of the worm indicates, appears to be complete at about the eleventh day, the only changes occurring after that being a lengthening and narrowing of the filaria, which enables it to enter the labium of the mosquito.

## II.

### *The Occurrence of Entamœba coli in the Human Intestine.*

When Schaudinn in 1903 separated and described two species of amœbæ infecting the intestine of man—one pathogenic, which he named *Entamœba histolytica;* the other non-pathogenic, which he named *Entamœba coli*—the writer was in charge of the bacteriological laboratory of the United States Army General Hospital at San Francisco, where hundreds of cases of amœbic dysentery, returned from the Philippines, had been observed, and where there were abundant opportunities for the study of the amœbæ found in man. After a year's study of the amœbæ found in patients suffering from amœbic dysentery and those occurring in the healthy bowel, including experiments upon kittens with both organisms, the writer published a paper confirming Schaudinn's results, in which the following deductions were made:—

(1) The intestine of man may be infected with two varieties of amœbæ—one pathogenic (*E. histolytica* or *dysenteriæ*), and the other non-pathogenic (*E. coli*).

(2) *E. coli*, the non-pathogenic variety, was found in 60 per cent. of the healthy individuals studied, and in 50 per cent. of individuals suffering from diseases other than dysentery.

(3) These two varieties of amœbæ can be distinguished in both fresh and stained specimens of fæces.

(4) They differ markedly in their method of reproduction, and this constitutes the most important method of distinguishing them.

(5) *E. histolytica*, whether fed in milk or injected into the rectum of kittens, produces the typical lesions of dysentery, as observed in man.

(6) *E. coli*, whether fed in milk or injected into the rectum, is absolutely harmless to kittens.

(7) Neither feeding experiments, nor rectal injections of fæces for the bacteria occurring in fæcal matter, result in the production of the lesions of amœbic dysentery, unless *E. histolytica* be present. One of the first subjects we investigated in the Philippines was the occurrence of amœbæ in healthy individuals and their morphology compared with that of the amœbæ occurring in patients suffering from amœbic dysentery. In all we examined 107 healthy members of the Hospital Corps of the Army; 71 per cent. were found to be infected with the non-pathogenic *E. coli*, while two were infected with *E. histolytica*. None of these men, with the exception of the two showing the dysenteric amœbæ in their fæces, had diarrhœa or dysentery at the time of examination, and all denied that they had ever suffered from dysenteric symptoms. Six of the men stated that they had had slight diarrhœa at times, always traceable to indiscretions in eating or drinking, but that they had never been on the sick list for it. The two men showing *E. histolytica* in their fæces were apparently in good health, but enquiry

elicitated the information that both were suffering from dysenteric symptoms at the time of examination and both were later returned to the United States with chronic amœbic dysentery. At the time that we examined the fæces of these men we knew nothing of the presence of the dysenteric symptoms, and our diagnosis was based entirely upon the morphology of the amœbæ observed in their fæces. It will thus be seen that, contrary to the opinion of certain investigators, it *is* possible to differentiate *E. histolytica* in fæces from the harmless *E. coli*.

In order to ascertain how long infection with *E. coli* might last, the following examinations were undertaken upon men who had been previously examined with a positive result, and who were still upon active duty at the hospital.

Upon November 20, 1906, eighteen out of twenty-three examined, or 78 per cent., were still positive for this parasite.

These examinations were divided as follows :—

(1) Eleven men were re-examined, eight months having elapsed since the first examination; nine, or 81·8 per cent., still showed *E. coli*. Not one of these men had suffered from the slightest diarrhœa during this time, and all had been on duty continuously at the hospital.

(2) Five men were positive for *E. coli* upon May 2, and were still positive upon November 20, 1906. No symptoms of dysentery were present during the time, not even the slightest diarrhœa.

(3) Five men were positive for *E. coli*, July 10, and two were still positive upon November 20, 1906. Neither of these men had suffered from diarrhœa or dysentery during this time.

As the result of our work along this line we concluded that in the Philippine Islands a very large proportion of

white men are infected with *E. coli*, and that such infection, so far as we have been able to observe, does *not* result in symptoms of diarrhœa or dysentery; in many of the cases the amœbæ disappeared, but in the large proportion this harmless parasite may be found even after the lapse of nine months, during which time the infected individuals remained in perfect health. The writer has been able to demonstrate this harmless amœba in his own stools for over four years, during which time he has never suffered from diarrhœa or any symptoms suggestive of amœbic dysentery. Schaudinn found this amœba present in 50 per cent. of healthy individuals examined in West Prussia, in 20 per cent. examined in Berlin, and in 66 per cent. of those examined along the shores of the Adriatic; the writer, in 65 per cent. of healthy American soldiers examined at San Francisco; Ashburn and the writer, in 71 per cent. of healthy American soldiers examined in Manila; and Vedder in 50 per cent. of American soldiers and in 72 per cent. of Filipino scouts in Mindanao, P. I. These observations certainly prove that *E. coli* infections are very common, do not result in dysentery, and that the parasite is detected with little difficulty after the administration of a saline cathartic.

We also concluded that *E. coli* differed very markedly from *E. histolytica* in its morphology and that it is possible to distinguish these two species of amœbæ by their morphological characteristics, if they be observed in fresh specimens of fæces and in properly stained preparations. In conclusion we say "we do not believe that the very large proportion of infections with *E. coli* which we have demonstrated can be explained by the theory of 'latent dysenteric infection,' but only, as we have stated in a previous report, by the fact that the non-pathogenic

*E. coli* is the organism present in these cases instead of the pathogenic *E. histolytica.*"

## III.

### *The Etiology of Dengue.*

Having been instructed by the Surgeon-General to investigate the etiology of dengue fever and to determine the possibility of the transmission of the disease by the mosquito, as claimed by Graham, of Beirut, we took advantage of an extensive outbreak of the disease at Fort Wm. McKinley, five miles out of Manila, to make the experiments, a *résumé* of which is here given. It is unfortunate that Graham also announced the discovery of a protozoon in the blood, for, while the method of transmission has been confirmed, no observer has been able to confirm the existence of a parasite in the blood of dengue fever.

It is rather surprising, in view of the scientific interest and importance of this question, that so little has been done to prove or disprove the results claimed by Graham from his mosquito experiments; it is not, however, surprising that those who have attempted to solve the problem have met with so little success, for only those who have done so can realise the difficulties and disappointments which await the investigator. In our work upon this phase of the subject the experimental results obtained, while proving that *Culex fatigans* (Wied.) transmits dengue fever, have been, at times, most disappointing and discouraging ; unknown natural conditions appear to be necessary for the transmission of this disease by the mosquito, and because of our ignorance of the method of securing these we believe that experimental transmission by the mosquito is rendered more difficult,

and that negative results may be expected more frequently than positive ones.

We have studied the blood of a large number of our cases during every period of the disease, but especially during the first two days and during the terminal rise in the temperature; various staining methods were used, including Wright's stain, and those used in demonstrating *Treponema pallidum*. The latter methods were used very carefully and in numerous cases, as, at the time we began our work, we were greatly inclined to believe that the organism concerned in the etiology of dengue might belong to the *Spirochætæ*.

From our examinations of the blood of dengue patients we considered that the following conclusions were justified :—

(1) There does not occur in the blood of dengue patients any visible organism, either bacterial or protozoal in nature, which can be considered as the cause of the disease.

(2) Dengue is not accompanied by anæmia, the red blood count being normal in uncomplicated cases. There are no characteristic morphological changes in the red corpuscles, leucocytes, blood plates or blood plasma.

(3) Dengue *is* characterized by a leucopenia, and in the vast majority of instances by a decrease in the polymorphonuclear leucocytes and a marked increase in the small lymphocytes; the increase in the small lymphocytes is constant throughout the disease.

*Blood Cultures.*—With the exception of McLaughlin, who found a micrococcus in his blood culture, we were unable to find that any investigator had cultivated an organism from the blood of dengue patients. McLaughlin's cultural methods were open to many objections and his results were of little scientific value.

We therefore approached this portion of our task with high hopes that by applying modern cultural methods we might be able to isolate and cultivate the organism causing this disease. In view of the success attained by Novy and others in the cultivation of trypanosomes, and by Rogers in cultivating *Leishmania donovani*, we were especially hopeful that by applying similar methods in this disease we might be able to secure growths of any protozoon which might be present. Although we gave all the modern methods of cultivation an extended trial, we were unable to confirm McLaughlin's results, and we concluded that no organism had any etiological relationship to the disease. In none of the cultures was a protozoon observed, and although some of the cultures were kept for two months, they remained bacteriologically sterile.

*Inoculation Experiments.*—We next directed our attention to the possibility of producing the disease by the inoculation of blood from dengue patients into healthy men; and as we were dealing with a disease which, in the young and robust, is not dangerous to life, we felt justified in making such experiments. We hoped in this way to determine the presence or absence of the infective agent in the blood, for should such experiments prove successful they would conclusively demonstrate that the cause of dengue is present in the blood, and that, therefore, insect transmission is possible, whereas negative results would prove that the blood does not contain the organism, unless it be one that first has to undergo a developmental cycle outside of the body, as in an insect, before it can produce the disease in man.

In order to secure subjects for these experiments a call for volunteers was issued to members of the Army Hospital Corps, serving at the Division Hospital, Manila,

and four men volunteered, in all of whom we succeeded in producing dengue by the intravenous inoculation of blood from cases of the disease. As more men were needed, and as no more Hospital Corps men were available, we consulted Major-General Leonard Wood, United States Army, commanding the Philippines Division, who authorized us to offer a reward for volunteering, as a result of which we secured many more than the fourteen men we needed. Unfortunately, of the fourteen men we experimented upon, seven came from Fort William McKinley, having passed unharmed through the dengue epidemic at that post, and of these men we found two absolutely immune, three relatively immune, and one doubtful. Of the same number of Hospital Corps men who had not been exposed to dengue, we found only one immune.

Eleven of our fourteen volunteers were given intravenous inoculations of unfiltered blood obtained from dengue patients, and of these, seven developed the disease, while in one case the result was doubtful. In three of the negative cases there existed, apparently, an absolute immunity to the disease. It was thus proved by us that the intravenous inoculation of unfiltered dengue blood into healthy men is capable of producing a typical attack of dengue.

Next, in order to determine if dengue belonged to the class of ultramicroscopic infections like yellow fever, rinderpest, &c., we determined to try the effect of the intravenous inoculation of filtered blood from dengue patients into healthy men. We experimented in this way upon two men in both of whom we were successful in producing very typical attacks of dengue accompanied by rather severe symptoms.

In our experiments we employed a Lilliput diatoma-

ceous filter, which was tested each time it was used, by filtering through it a suspension of *M. melitensis* and *S. choleræ*, the filtrate being incubated for two weeks afterwards. The filter used retained both these organisms, the filtrate always remaining sterile. Besides the control test of the filter, we kept in each case a portion of the filtered dengue blood for a period of ten days, making daily examinations, but no growth was ever obtained from the blood or in cultures made from it. We regard the two cases of dengue produced by the intravenous inoculation of dengue blood as typical of a severe type of the disease; and we believe that these two experiments prove conclusively that dengue can be transmitted by blood which has been passed through a filter fine enough to retain organisms 0 4 micron in diameter (the measurement of *M. melitensis*). It also proves that, in all probability, the causative agent in dengue is ultramicroscopic in size, for the reason that neither in fresh nor stained blood smears, nor in the filtrate obtained from dengue blood, can any organism be demonstrated by the microscope. This conclusion explains the uniformly negative results obtained by nearly every observer in the search for a dengue parasite in the blood.

We concluded that an organism was present in the filtrate rather than a toxin, because of the length of the period intervening between inoculation and the appearance of clinical symptoms, and also because we have reproduced the disease by the inoculation of the blood of patients who had been infected by filtered blood.

*Experimental Transmission of Dengue by the Mosquito.*—Since the positive results obtained by Graham in his experiments regarding the transmission of dengue by the mosquito, *Culex fatigans* (Wied.), several investigators

have endeavoured to confirm his statements, but have been unsuccessful. However, to one who carefully studies the epidemiology of dengue, the conclusion is almost inevitable that this disease, which so closely resembles yellow fever and malaria, must be transmitted by some species of mosquito. Its seasonal prevalence; its frequent occurrence along low-lying, moist, coast regions, and in the valleys of rivers; its rapid diffusion in certain localities and its lack of diffusion in others; its relation to changes in temperature and moisture; its manner of spread from building to building in infected places; the presence of multitudes of mosquitoes wherever dengue is present, and the absence of the disease in regions where mosquitoes are few in number or absent, and the cessation of the epidemic in badly infected districts when conditions arise unfavourable to the propagation of mosquitoes, all point to some species of this insect as the transmitting agent.

In looking over the geographical distribution of dengue and various species of mosquitoes, we found but one species (*C. fatigans*, Wied.) of this insect that apparently occurred wherever dengue did. This species is constantly found in dengue-infected districts, and it is mentioned by almost every investigator as being very numerous during epidemics of this disease. In Theobald's monograph the map illustrating the known distribution of *C. fatigans* might almost be used to illustrate the distribution of dengue fever, and, if to this map be added the regions in which this mosquito has been demonstrated since it was published, the association of dengue and *C. fatigans* is still more striking. For this reason, and because this mosquito was employed by Graham, we decided to work with this species at first, and in the event of our results being negative, to extend our work to embrace other species.

Unfortunately for the fullest success of our work in this direction we were forced to employ in our experiments a number of men who had already passed through the epidemic of dengue at Fort Wm. McKinley and the majority of whom were immune, as proved by the intravenous inoculation of dengue blood. Thus of the nine men used, only four were found susceptible to the disease, and of these one developed a typical attack of dengue following the bites of infected mosquitoes (*C. fatigans*). This case was in every way typical of a moderately severe attack of dengue, the symptoms being those usually observed in the great majority of naturally acquired infections, and the temperature chart was a very characteristic one. This man had not been exposed to dengue before being bitten, living in a mosquito-proof tent for some time before the infected mosquitoes were allowed to bite him.

Since our work was completed as regards insect transmission our results have been confirmed by a Board of Army Medical Officers, and in localities infected with dengue the Government has ordered that all barracks and quarters be screened.

As regards the *period of incubation* in dengue, our experiments show that in cases of the disease produced by the inoculation of dengue blood, the period of incubation varies from two and a half to seven days, the average being about three days and fourteen hours. This agrees closely with the period of incubation observed in naturally infected cases. We observed no case in which the period of incubation was as short as twenty-four hours.

*Contagion in Dengue.*—We very carefully studied the question of contagion in dengue and believe that the following facts conclusively prove that dengue *is not* contagious in the slightest degree :—

(1) At the hospital at Fort Wm. McKinley over 600 cases of dengue were treated in the general wards without a single case originating among the other patients in the wards. Only four men belonging to the Hospital Corps, on duty at this hospital, contracted the disease, three of them being nurses on night duty in the wards, and the other a cook, having no contact with the dengue patients. No precautions were used to prevent contagion beyond the rigid use of mosquito bars at night, the dengue and other patients eating together and being closely associated throughout the day. It is noteworthy that the only men unprotected by the mosquito bars at night—that is, the three night nurses—all developed the disease.

(2) In our dengue camp where we treated over 120 cases, no instance of infection occurred among the attendants, although their association with the dengue patients was very intimate and extended over four months; mosquito protection was the only means used to prevent infection.

(3) Our experiments with fomites were all negative. We endeavoured to produce the disease by exposure of healthy men to fomites, the men living in mosquito-proof tents with patients suffering from dengue, throughout the entire course of the disease. They slept in the beds of the dengue patients, wore their underclothing and pyjamas, and ate and drank from the same table. In this way we experimented with eight men, none of whom developed the disease from such exposure.

We concluded, therefore, that dengue is not a contagious disease, and that patients suffering from it may be placed in the general wards of a hospital without fear of infecting other patients, provided precautions are taken against the bites of mosquitoes.

It is interesting to note the close analogy of this disease with yellow fever, with which it is often confused in regions where both occur. It will not be strange if later investigators demonstrate that both are due to very closely related organisms, probably protozoal in nature, perhaps differing only in virulence, as is the case with the tertian and æstivo-autumnal malarial plasmodia.

## IV.

### *Treponema pertenuis and the Production of Yaws in Monkeys.*

In closing this *résumé* of the work of the Tropical Board a brief synopsis will be given of our investigations regarding the etiology of framboesia or yaws, and the experimental production of this disease in monkeys.

In February, 1905, Castellani, while investigating the etiology of yaws at Colombo, Ceylon, discovered a spirocheta in the serum of yaws lesions, resembling very closely *Treponema pallidum* in its morphology. He named the organism *Spirochæta pertenuis*, but as it undoubtedly belongs to the genus *Treponema*, the correct name is *Treponema pertenuis*, Castellani. At the time of our investigations, only a few confirmatory reports had appeared, and no work which was conclusive in character had been done upon the experimental production of the disease in monkeys.

We examined the serum from the yaws papules of ten cases for *T. pertenuis*, finding the organism in all of them. In morphology the parasite is, we believe, indistinguishable from *T. pallidum*, and its staining reactions are the same. The length and number of the curves vary greatly, the average number of curves being

eight, but as many as seventeen have been counted in one organism. In neither fresh nor stained specimens were we able to observe anything which could be interpreted as an undulating membrane, nor anything that was differentiated as a flagellum in the distinct manner in which flagella are differentiated on certain species of bacteria. The motility of the organisms observed in fresh specimens of the serum varied from a darting movement so swift as to be almost invisible (the appearance being similar to that of a glancing light) to a very sluggish motion, which so closely simulated entire passivity as to leave the observer in doubt as to whether it might not be due to currents in the serum. When the organism can be well seen and clearly identified the motion is always slow, consisting of a rotation upon the axis of the spiral, giving the so-called "cork-screw motion," and a gentle waving and bending of the entire organism.

As regards *division*, we believe from our observations that, as a rule, multiplication occurs by *longitudinal* division.

The motility we found to be retained in capillary tube preparations of the serum for a period of several days, but it becomes sluggish after a few hours. In one instance we found treponema showing slight movement after thirty-four days in a capillary tube preparation of yaws serum. In this tube no other organisms were present, a pure culture of the treponema, in which some multiplication appeared to have occurred, being obtained.

*Cultivation.*—At the suggestion of Dr. Miyajima, of the Imperial Institute of Tokio, the study of these capillary tube preparations was undertaken in order to observe the phenomena of agglutination, which he said

he had obtained in similar preparations of *T. pallidum*. We found that, in such preparations, *T. pertenuis* agglutinated very promptly, large clumps being formed within twenty-four hours. We found, in addition, that an apparent marked increase occurred in the number of organisms in such preparations—an increase usually manifest within twenty-four hours, but sometimes becoming marked only after several days. We believed that an undoubted multiplication of the treponema occurred in the serum tubes, as well as agglutination. We obtained similar results in the case of *T. pallidum* from one case of syphilis.

*Inoculation in Animals.* — It has been stated by different authors that yaws is inoculable on the lower animals, notably cats and monkeys, and that it is inoculable from person to person. We made no inoculation experiments on men, and none on lower animals other than monkeys (*Cynomolgus philippinensis*, Geoff.). Of these we inoculated five, using serum from the yaws tubercles of three different patients. All five of the monkeys developed yaws lesions of a sufficiently characteristic appearance to permit of diagnosis based upon the clinical features alone. In addition to this typical appearance of the lesions we found *T. pertenuis* in all the lesions. The organisms did not differ in any demonstrable way from those observed in the serum from human lesions. In numbers, measurements, staining reactions, shape and motion, they were similar. In all, eleven monkeys were used in our experimental work. Of these, five were inoculated directly with serum from a human lesion; one with serum from a human yaws lesion, the serum having been kept in a glass capillary tube for three days; one was inoculated with blood from the heart of a monkey that had developed yaws;

one with splenic juice from the same monkey; one with serum from a yaws papilloma in a monkey; and two with serum from a primary syphilitic lesion. In addition, one monkey, after recovery from yaws, was re-inoculated with human yaws serum, and two after recovery from yaws were inoculated with syphilis.

As regards results: Of the five monkeys inoculated with human yaws serum, taken immediately from the yaws lesion, all developed typical yaws tubercles; the animals inoculated with the heart blood and splenic juice did not develop yaws—the animals re-inoculated with yaws serum, after recovery from yaws, did not again develop the disease; the two animals which had recovered from yaws, and were inoculated with syphilis, did not develop syphilis, nor did two control monkeys inoculated with the latter disease develop it. It has been found impossible to inoculate syphilis in the species of monkey used in our experiments.

The *period of incubation* in our experimental yaws monkeys varied from sixteen to forty-five days, but it should be understood that this is only approximate, as owing to the distance of the animals from us and pressure of work they were not inspected every day, and thus the lesions may have existed for a short time before they were noticed. The average period of incubation was twenty days.

As regards *duration of the disease* in monkeys, it varied from two weeks to eighty-four days. In the five monkeys in which we produced yaws by inoculation the duration of the lesion was as follows: Monkey No. 1, eighty-four days; monkey No. 2, fifty-seven days; monkey No. 3, ten days (this animal was chloroformed while the lesion was still active); monkey No. 4, thirty-nine days; monkey No. 5, fourteen to twenty-one days. It was our

experience that in the more severe cases the primary lesion tended to spread into the surrounding skin, and the more marked this tendency was, the longer the disease lasted. We failed to observe any glandular enlargement, or any symptoms pointing to a general infection. The lesions produced by experimental inoculation in monkeys did not differ essentially, in their morphology, from those occurring in the disease in man, but we never observed the secondary or generalized eruption, which, according to most authors, follows the primary lesion in the human subject.

We examined the lesions of all of our successfully inoculated animals for the treponema, and repeatedly demonstrated its presence in every case, without difficulty. The organisms could be found in the very earliest stage of growth of the yaws papule and they persisted until the lesion had nearly healed, being most numerous during the active growth of the papule and decreasing in number as the healing process advanced. Serum from the lesions in some of our inoculated monkeys was collected in capillary tubes and kept for varying periods of time; apparent multiplication of *T. pertenuis* occurred in some of the tubes and the organisms remained motile for several days. They occurred in pairs, in clumps, and singly. Agglutination and longitudinal division were also observed in the serum from the lesions of these animals.

We concluded that this organism is the cause of yaws because of its constant presence in the lesions of man and in those of monkeys, produced by the inoculation of yaws serum from human cases, and their absence in other conditions, added to the fact that, as the experimental lesions heal, the treponema gradually disappears. Moreover, treponema is not found in pyogenic ulcerations

in monkeys suffering from yaws, as proved in one of our experimental animals, in which at the site of the yaws inoculation such an ulceration appeared, but no yaws lesions developed. This species of treponema we found constantly and only in the lesions of yaws or frambœsia, whether the lesions were observed in man, arising from natural infection, or in monkeys, arising from infection with the yaws serum of human cases.

As the result of our work we concluded that *T. pertenuis* is the cause of yaws; that it reproduces by longitudinal division; that it is constantly present in the serum from the yaws lesion; and that the inoculation of such serum, subcutaneously, or by rubbing it into an excoriated portion of the skin of monkeys (of the species used), is followed by the appearance of typical yaws papillomata at the site of inoculation, in the serum of which treponema is easily demonstrated. Also that this organism and *T. pallidum* may be differentiated by the results obtained from the inoculation of monkeys, and that yaws and syphilis are distinct diseases.

In concluding this paper, the writer would ask the Fellows of the Society to bear in mind that the observations noted were made by Major Ashburn and himself, and that a large portion of the paper is abstracted from reports published in the *Philippine Journal of Science*, and in other periodicals, where exact details are given of their experiments and results.

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## Discussion.

Dr. G. C. Low said that in the first place their thanks were due to Dr. Craig for his kindness in sending them the very interesting paper they had just heard. His own remarks would be limited to the first part, namely,

the section which dealt with a so-called new filaria (*Filaria philippinensis*). Lately there had been a tendency, especially in protozoology, to create new species on what, at least to the scientific mind, were very insufficient grounds, and one sincerely hoped that a similar tendency was not going to make its appearance in helminthology. To his mind, the arguments brought forward by Dr. Craig for differentiating this filaria from the ordinary embryos of *F. bancrofti* were totally insufficient. He granted that there might possibly be different species included under the name *Microfilaria bancrofti vel nocturna*, but before they could be accepted as new there must be positive proof. At a recent meeting this question had been discussed, when Dr. Leiper stated that too much stress should not be laid on embryonic characteristics in determining species. In the speaker's reply he admitted this, at the same time, however, showing that where the embryo was manifestly different it did prove that the adult must also be so, and was a good argument for the determination of a new species. Actual examples of this had happened in the case of the embryos of *F. perstans* and *F. demarquayi*, which were rightly separated by Manson from *F. bancrofti* before their adults were found. That was a very simple case, however; when it came to saying that embryos, which were identically the same microscopically, belonged to a different parent, difficulties arose; for example, the question of *F. ozzardi* being the same as *F. demarquayi*, or the question of different species existing under the name of *F. bancrofti*, could not be settled in that way.

Apparently what led Dr. Craig to think that he had found a new filaria was the erroneous supposition that filariasis did not exist, or was very rare, in the Philippines. This, his successors, as Dr. Craig himself

admitted, had shown not to be the case, and the explanation of this was simply that no one with the requisite knowledge had looked for it before. Next, the fact of embryos being seen in the blood by day aroused Dr. Craig's suspicions. There was nothing specially peculiar, or one might say new, in this alternation or irregular periodicity; it had been described by many before and was a well-known fact to all who had worked on the subject. Further, the technique employed to demonstrate the periodicity as described in the paper was faulty to a degree. He (Dr. Low) had already pointed out in a paper on *F. perstans*, that, in experiments undertaken to estimate the number of embryos in the blood at any given time, measured quantities of blood must be taken; this was not done in the present instance, and, as far as one understood the paper, the exact hours at which the different examinations were made were not given.

Passing to the description of the embryos, there was nothing to show that they differed from the embryos of *F. bancrofti*. They measured 0·32 to 0·29 mm. in length by 0·0065 mm. in breadth—figures that applied equally to the embryos of the latter species. They were sharp-tailed, sheathed, with a cephalic armature, characteristics which were also common, and the only difference one could detect was that they were described as locomoting; but then there was no proof that they had not come out of their sheaths. If they had done so, they would be exactly similar to *Microfilaria bancrofti*. *C. fatigans* was the chief intermediate host for the embryos of *F. bancrofti*; here again it acted for the new species, and what was still more strange no differences in their development in that insect to that of the former could be detected. Adults were not found, and without them the gap in the chain of evidence was

much too wide to allow of the statement that a new species of filaria had been found. The only striking difference, and he had shown that that was not a real one, was periodicity; with the anatomy and other points corresponding absolutely as they did, that was not enough. The name *F. philippinensis* must therefore go, or become a synonym of *Microfilaria bancrofti*. So they would have *F. bancrofti;* embryonic form, *M. bancrofti;* synonyms, *F. sanguinis hominis, F. nocturna, F. philippinensis.*

Dr. SANDWITH said the question of the etiology of dengue had always been of very great interest to him because he used to be convinced that the disease was a contagious one. But at the Medical Congress in Cairo in 1902 a paper had been sent to him by Dr. Harris Graham describing his (Dr. Graham's) experiments upon the transmission of the disease by means of the mosquito. Dr. Graham took some mosquitoes infected by dengue patients to a high altitude where there was no dengue, and there infected some villagers who had never heard of the disease, and he (Dr. Graham) proved that *Culex fatigans* was the transmitting agent of dengue. Since then it had been generally recognized that this was the mode of transmission, and Captain Craig's paper was interesting as confirming this. It added another to the diseases to which man was liable from his extraordinary habit of encouraging the growth of the mosquito instead of killing it on sight. In spite of the experiments of Graham in 1901 dengue was not yet universally recognized as a disease transmitted by mosquitoes.

Mr. E. E. AUSTEN said he would like to suggest that there might, perhaps, be an insect other than the

mosquito which should be considered and examined in connection with dengue. Quite recently—within the last two months—a book had been produced by three surgeons of the Austrian Army on a disease called "Pappataci fever" which is endemic in the Adriatic Littoral of Austria-Hungary. This fever which temporarily incapacitates some 90 per cent. of the Austrian troops stationed in Bosnia and Herzegovina, has a very strong affinity to dengue, if indeed it be not a form of that disease. It had been proved conclusively by a series of

*Phlebotomus* sp. ♀, Kassala, Sudan. (× 12.)
Copied by permission from the "British Museum Instructions for Collectors," No. 7, 1907.

experiments that this fever was conveyed by a dipterous insect called *Phlebotomus papatasii* (specimens of which were shown). This genus (of which allied species occurred in several of our own Colonies) belonged to the family of *Psychodidæ*, or Sand-flies. Its body, wings and legs were all closely covered with hair (not scales as in the case of the mosquito, although allied to that insect); it was small, of a brownish-yellow colour, and varied in size from 2 to 3 mm. It had long legs, a long proboscis, long antennæ and long palpi, the palpi

being practically the same length in both male and female. The females bit and sucked blood, but only at night, and this fact was proved very clearly in the experiments conducted by the Austrian surgeons, who found that only troops who remained in infested stations at night suffered from the disease. If they were removed to the hills at night the disease did not affect them. This fever was of a type very similar to that which affected the British Army in India. According to the Medical Service Returns for the British Army in India, and also for the Mediterranean stations, there had been a large number of cases of fever admitted to hospital which represented in the aggregate an enormous loss of days of service, and he thought this fact alone was sufficient to justify the enquiry which was about to be made in Malta. From the investigations of the Austrian surgeons it appeared probable that *P. papatasii* bred in latrines: a species of the same genus which occurs in Ashanti was found to be very common in latrines. *P. papatasii* was extremely common all through Egypt, the Arabic for it being "akhl-uskut," meaning, he thought, "a thing which bites in the stillness of the night." There were reasons for believing that a species of this genus which occurred in India, and was found to be extremely common in certain stables, might have been responsible for an outbreak of surra among Tonga ponies. The outbreak carried off over one hundred animals, but ponies stabled at night in non-infected stalls did not contract the disease.

He mentioned this fact, not because it bore immediately on the point in question, but because surra was a disease which was believed to be conveyed by more than one insect; so also it might be that dengue was conveyed by *P. papatasii* as well as by *C. fatigans*.

Dr. SANDWITH said that the literal meaning of the Arabic word "ʻakhl-uskut" was "silent eater." It was the idea of natives that there were two kinds of insects—one the ordinary mosquito as they would call it, which makes a little pleasant humming noise, and another which bit without any premonitory sound.

Mr. AUSTEN said *P. papatasii* made no noise as it flew; species of *Phlebotomus* were commonly known to Englishmen as "Sand-flies."

Sir PATRICK MANSON said as regards *F. philippinensis* he agreed with Dr. Low, although admitting the possibility that there might be a new species of *Filaria* having the characteristics described by Captain Craig, yet the evidence so far produced was not quite sufficient to justify any positive statement on the subject.

He wished someone had spoken on the subject of *Entamœba histolytica* and *E. coli*, because his (Dr. Craig's) observations were so much at variance with those of his colleagues in the Philippines, Drs. Musgrave and Strong, and Dr. Wenyon, who refused to admit the description of the *E. histolytica*.

With regard to dengue fever he always taught that Graham had stated that *C. fatigans* was the transmitter of dengue fever, but that the case was not yet completely proved against the mosquito. He thought the analogy strongly suggested such an etiology. The number of cases put forward by Dr. Craig were just sufficient to encourage further experiments, but they were not sufficient to justify the statement that mosquitoes were the transmitting agents of dengue fever.

He thanked Mr. Austen for his interesting remarks on *P. papatasii* in connection with an epidemic fever occur-

ring in Bosnia and Herzegovina. He had no doubt that in the future there would be abundant opportunity for further investigation.

As regards the paper upon the *Treponema pertenuis*, he was glad to hear that Dr. Craig had been able to confirm Castellani's experiments. If his (Sir Patrick Manson's) recollection was correct, Castellani had succeeded in giving not only a local disease to monkeys, but also in getting monkeys to develop a manifestation of yaws.

# A CASE OF MALTA FEVER FROM NORTHERN NIGERIA.

By GEORGE C. LOW, M.A., M.B.

Malta fever has long been known to exist in other parts of the world than the Mediterranean, cases recently having been reported from India, South Africa, the Sudan, and elsewhere, so there is nothing remarkable in the fact that it should also occur in Northern Nigeria. Whether or not it should prove to be common there remains to be seen, but certainly since I saw the gentleman (in 1906) whose case I am about to read to you to-night, I have not heard of any others till the one Sir Patrick Manson had under his care at the end of last year. This case of Dr. Foy's in Northern Nigeria is also to be read to you to-night, and perhaps when some prominence has been given to the subject other cases of obscure and prolonged fever from these parts may turn out to be the same disease. The notes of my case are as follows:—

*Case of Mr. G.*—A former patient of Dr. Blair's in Northern Nigeria was under the care of Dr. Cardell at Tonbridge, and I saw him in consultation with the latter on July 18, 1906. Dr. Blair had before this seen Mr. G., who was suffering from fever, and had ordered intramuscular injections of quinine on the assumption that the illness was malarial fever, but this treatment had absolutely no effect on the temperature.

*History of Case.*—Patient had served in the South African War in 1898, and after that had done three tours on the West Coast of Africa—the first to Sierra Leone, the second and third to Northern Nigeria. In the last of these he was chiefly stationed at Kano, but had been on an expedition to Sokoto in March, 1906, and after that

on another one to Hadeija in April of the same year. After this he proceeded down country to go home on leave. During his stay on the coast he had enjoyed fairly good health all the time with the exception of one or two slight attacks of fever, which responded to quinine. He had been in the habit of taking 10 grains of quinine every second day as a prophylactic during his first two tours, but latterly took it irregularly. He was always careful about sleeping under a mosquito net, and was never conscious of having been specially bitten by tsetse or other biting flies.

*Previous Illnesses.*—Slight touches of fever as above. Slight dysentery in South Africa in 1898. No blackwater fever. No syphilis.

*Present Illness.*—This began indefinitely. Fever was apparently contracted on coming down to the coast from the interior in April, 1906, and this resisted quinine. On account of this he was kept in hospital for a week at Zunguru, but the temperature still persisted. Afterwards he reached the coast and took ship for England, the sea air reviving him considerably and causing his fever to disappear after a week on board. When he landed in England he felt well. On July 7, 1906, he was at a cricket match, the day being very warm, and in the course of the afternoon he began to feel chilly and seedy, so he went home to Tonbridge that night. Since that day continuous fever set in, five intramuscular injections of quinine and plenty of quinine by the mouth having no effect on the temperature.

*State on Examination* (July 18, 1906).—The patient looked somewhat sallow, was not in the least apathetic or dull, conversed sensibly, and did not strike one as being specially ill. His temperature was 102·5 F., Dr. Cardell stating that it usually ran up to 103 or so at

nights, falling to 100° or 99° in the mornings. The pulse was slow in comparison, 82 during examination. There was nothing specially abnormal in any part of his system. The tongue was small, heavily furred and dry. The liver was perhaps slightly enlarged, its upper border being at the fifth and sixth ribs, its lower border at the costal margin, edge not palpable. The spleen was also slightly enlarged, especially upwards, its upper border being at the seventh rib, its lower at the eleventh; it could not be felt. An examination of his blood gave the following count :—

| | | |
|---|---|---|
| Reds .. .. | 4,060,000 | No parasites of any kind found. |
| Whites.. .. | 7,500 | |
| Hb. .. .. | 75 per cent. | |
| Differential : Polymorphonuclear .. .. | 40 per cent. | |
| Large mononuclear .. .. | 11 ,, | |
| Lymphocytes .. . .. | 45 ,, | |
| Eosinophile .. .. .. | 1 ,, | |
| Transitional .. .. .. | 2 ,, | |
| Mast cells .. .. .. | 1 ,, | |
| | 100 | |

What might have been three spots were noted on his abdominal wall, but they were doubtful and uncertain. From the blood count the case was evidently not an abscess of the liver; malaria was negatived by the failure of intramuscular quinine to influence the temperature; trypanosomiasis, typhoid, tuberculosis, and Malta fever remained. Of the first of these there were no confirmatory signs such as enlarged glands or erythematous eruption on body; it looked more likely, then, that the patient was suffering from a very mild attack of typhoid fever, though several things were against this, especially the previous fever in Africa and the cheerful condition, as if there was little the matter with him. Blood was taken back to London for the Widal reactions; these were done on July 19, dilutions of 1 in 25 and 1 in 50 being abso-

lutely negative for typhoid, while for Malta fever there was a suspicion of clumping, but as this was not altogether satisfactory I gave it as negative. More blood was sent the following week, and on July 25 the Widal for typhoid was again negative; that for Malta fever was positive in dilutions of 1 in 25, 1 in 50, and 1 in 100. Dr. Cardell also reported on this date that the temperature continued the same, but the patient had had an unexplained pain in the left maxillary joint (supposed to be rheumatism). The blood was sent again the following week, and it reacted very strongly for Malta fever in dilutions of 1 in 50 and 1 in 100. Dr. Blair again saw the patient on August 10 and found the temperature still remaining the same and no fresh developments. It was clear, then, that the case was one of Malta fever, and I directed that the case should be treated as such. I did not see the patient again nor hear of him until I saw Dr. Blair in January, 1908, when he told me that the patient had remained ill till the late autumn of 1907, *e.g.*, well over a year, when he slowly regained his health, and was then (January, 1908) in perfect health. The long duration of the disease was of course a strong point in favour of the original diagnosis, if that were required. No cultures were made from the blood for the micrococcus, and one or two other minor points are wanting in the clinical history, but there is no doubt that the case was one of Malta fever, and it shows that this disease is present in Northern Nigeria, as well as in other parts of Africa.

## A SECOND CASE OF MALTA FEVER FROM NORTHERN NIGERIA.

By H. A. FOY, L.R.C.P., L.R.C.S.Ed.

Mr. J. H. G., aged 30, admitted for fever at Maifoni, South Bornu, on June 24, 1908.

*History.*—On June 22 felt ill, but ten days previously to this felt indisposed and unfit for work.

*Habits of Life.*—Regular smoker, alcohol in moderation, has taken quinine daily in "tabloids" regularly since middle of January, 1908.

*Residence.*—Present tour in Northern Nigeria dates from October 15, 1907. Previous to this spent two years in England, after a tour of thirteen months in Southern Nigeria.

*Previous Illnesses.*—In the early part of his present tour, while stationed at a place called Akwacha in the south of the Protectorate, he had three small attacks of malarial fever, each lasting a couple of days. Had another attack of malaria on January 12, when on his way up to Maifoni, where he kept good health. From the middle of May to June 7 went into the district to relieve a detachment where his water supply was not very good, and he drank unboiled milk. There he had diarrhœa, two to three motions a day. The onset of his present illness was fifteen days after his return.

*Condition on Admission.*—Well-nourished young adult. Physique good. Temperature 100° F.; pulse 80.; respiration 16. Organs healthy.

Digestive System: Tongue coated, loss of appetite, bowels constipated. Fæcal examination: Anguillulæ and ova of *Trichocephalus dispar* present.

Nervous System : Constant headache, with spasmodic exacerbations when pain became very intense, radiating forwards from the parietal area to the forehead, intolerance to light, pupils contracted, insomnia marked.

The urine contained urates, but no albumen nor sugar.

Sweating was a marked feature throughout the first two weeks, and after a few days gave rise to a great outbreak of sudamina and erythema.

The blood examination of fresh specimens and of stained films gave no information; no malarial parasites were seen.

The initial rise of temperature resembled a miniature chart of enteric fever, only that the duration of the wave of fever was not that of typical enteric, for the morning temperature began to decline on the eleventh day of the disease, and the temperature became practically normal by the eighteenth day. The maximum temperature reached during the first week was 103·4° F. Later, by July 23, he again had a low wave of temperature for eleven days; then again normal for two days, when on August 6, a third wave of low temperature began, lasting twenty days, up to August 26, when it again fell to normal, and the patient was now on his way to England. A slight spell of temperature again occurred on September 4, lasting three days, and again later for a few days during the voyage to Plymouth. He arrived there on October 1, when he came to London, and was subsequently under the care of Sir Patrick Manson. During the voyage home the patient did not gain in strength and general health.

The other symptoms which occurred during the first week, and subsequently in the first stages of the attack, were as follows: Tongue remained coated, constipation continued up to the fifth day, and on the sixth day

diarrhœa supervened; there were five motions, the characters of which were that they were of liquid, thick, pea-soupy consistency, yellow and foul-smelling. The diarrhœa, to the extent of two or three motions a day, continued for nine days; and then the motions were reduced to one a day, which was often formed, but varied in consistency, was frequently coated with mucus, and occasionally streaked with blood. This latter state of the bowels continued until the patient left for England. The headache and restlessness with insomnia were marked features during the first eight days of the disease; pupils were at first contracted, and then gradually dilated. The spleen became enlarged.

*The Blood.*—On July 29, thirty-four days after the onset of the fever, specimens of blood were taken and sent to England. These were examined two months later by Dr. Low for the agglutination test for typhoid, with a negative result.

From the symptoms at the end of the first week, the diagnosis of a mild attack of enteric fever was made. It would be well to note that a most characteristic case of enteric fever had occurred four months previously in the station.

*Diagnosis.*—The points in favour of enteric fever at the end of the first week were as follows: Gradual onset; character of the fever; persistent headache and insomnia; contracted pupils followed by dilatation; slight bronchitis; early constipation followed by diarrhœa, the character of the motions resembling those of typhoid; and a comparatively slow pulse-rate.

*History of the Case after October* 1, 1908, *in London.*—A slight wave of temperature again occurred between October 2 and 5, then a period of normal temperature, up to the 19th, then again another rise lasting from

October 20 to November 15. Towards the latter part of this period of fever the temperature reached a maximum of 103·8° F., on November 9. During this attack of fever the blood was, on November 4, examined by agglutination test for Malta fever at the London School of Tropical Medicine, with a negative result. On November 6 the blood was again examined in detail by Dr. Low, with the following results :—

| Blood Count | | Differential Leucocyte Count | | Parasites |
|---|---|---|---|---|
| Red corpuscles | 4,750,000 | Polymorphonuclears | 52 per cent. | |
| White corpuscles | 5,600 | Large mononuclears | 1·4 ,, | |
| Hæmoglobin | 90 per cent. | Lymphocytes .. | 41·6 ,, | *Nil.* |
| | | Eosinophiles .. | 2·8 ,, | |
| | | Transitional .. | 2 ,, | |
| | | Mast cells .. .. | 0·2 ,, | |
| | | | 98·2 | |

Number counted—500.

*Agglutination Reaction.*—A positive reaction for Malta fever was obtained by Dr. Low on this occasion. On November 10 a tender spot appeared in the right thigh.

From November 16 to 21 another rise of temperature occurred. On November 17 a sample of blood was sent for the agglutination test to Dr. Nabarro at University College, and with it another sample of normal blood from a healthy person was sent as a control, with the result that the specimen from the patient gave a distinct positive reaction to Malta fever both microscopically and macroscopically, with dilutions of 1 in 250, whereas the control of normal blood gave a negative reaction.

Subsequently the blood was tested by the Clinical Research Laboratory, and by Fleet-Surgeon Bassett Smith, with a positive result.

Since December the temperature has run a fairly

normal course with occasional slight irregular rises, the general condition has improved much, the patient is no longer anæmic and has become stout, but his pulse continues to run high, ranging from 90 to 100 per minute, rising still higher to 120 or more on the slightest exertion. Taking into consideration the symptoms of the case as a whole, together with the chronic course run by the disease, which was marked by an initial spell of rise in temperature followed by several irregular relapses, although the initial attack of fever together with the other symptoms simulated a mild attack of enteric fever, it is practically certain that the case was one of Malta fever from the onset, as verified by the agglutination test. It is interesting to know in connection with this diagnosis that the unboiled milk which he drank some three weeks previous to his illness was goat's milk.

Dr. CHRISTOPHERSON said he would like to remark that the Malta fever he had met with in the Sudan had not been accompanied by sore throat nor pains in the joints which he understood were characteristic symptoms of Malta fever elsewhere.

Sir PATRICK MANSON said that the two cases of Malta fever referred to in the papers just read were of interest clinically, but more especially as they had proved that this disease was found in Northern Nigeria. The second case was of particular interest to him because he was originally not at all sure that it was not one of sleeping sickness. He examined the patient's blood microscopically from time to time, but he failed to find trypanosomes, and it was only after some considerable time that he thought it might be Malta fever. He confessed to a want of confidence in Widal's reaction as a possible means, in this country, of determining the diagnosis of

Malta fever, but in this case he (Sir Patrick Manson) got four positive reactions and one negative, and he thought that this, together with the clinical symptoms, was sufficient to establish a diagnosis of Malta fever. Some days ago he sent a patient's blood to Dr. Low for a Malta fever test. Dr. Low got a positive reaction 1 in 100, a very marked and rapid reaction, and so far as reaction was concerned the diagnosis of Malta fever was confirmed. But he suspected the case might be one of tuberculosis or syphilis instead of Malta fever, and he gave the patient iodide of potassium. He improved rapidly under this treatment and had remained well ever since, so that one could not be quite sure of the reliability of reaction tests under the conditions in which they were done in this country.

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# THE CAUSE OF TRUE OR TROPICAL BERI-BERI.[1]

By LEONARD BRADDON, F.R.C.S., Seremban.

*Read April* 16, 1909.

Beri-beri, properly so-called, is a disease of the Far East, of Japan and of the ports of China, and is especially prevalent in the British and Dutch Settlements and possessions throughout Malaya. Other morbid conditions which correspond clinically with beri-beri should not be regarded as identical with it, nor should any assemblage of symptoms be accepted as beri-beri unless it can be shown that the same pathogenic agent is involved.

*Epidemiology.*—Throughout the Dutch East Indies for 150 years, in Singapore and Penang for ninety years, and in the Federated Malay States for the last thirty years, beri-beri has been perennial, endemic, occasionally epidemic. In the British area, which has a population of some 600,000, the recorded deaths in hospitals from beri-beri amount to 2,000 annually, the cases admitted to hospital for treatment being four times that number. The records are therefore rich in facts available for evidence as to the etiology of the disease.

In this large area, and throughout this long period, in all the epidemics described, as well as in sporadic cases, there has been only one factor recognizable as common to all; among communities in places where that factor has been absent there has been no beri-beri.

All races are susceptible to beri-beri, and there is no difference in the degree of susceptibility.

In Acheen—a district of Sumatra practically identical

[1] The paper forwarded by Dr. Braddon has of necessity been considerably abbreviated.

with the Malay peninsula as regards climate and conditions of life—during the twenty-two years 1873-1895, out of an average strength of 15,200 Europeans (Dutch) in military employ no less than 17,520 were invalided for beri-beri, the mean attack-rate being 52 per 1,000. During 1883-1888 the case incidence was as high as 25 per per cent. of strength, although beri-beri was unknown locally. In British Malaya, during the same period, the European troops (most of them in Singapore, a notorious hotbed of beri-beri) were entirely free from it.

To explain the prevalence of beri-beri among the Dutch troops and its absence from the British, there must have been some unvarying difference of conditions. Race was not the factor as it affords no immunity; nor was place, as the British lived in a haunt of beri-beri. But there was one constant difference, viz., food. Rice formed the chief component—55 per cent.—of the diet of the Dutch soldiers in Acheen attacked by beri-beri; it is seldom eaten by the British troops in Malaya.

Had in any year one Dutch regiment serving in Sumatra been affected by the disease while a corresponding unit quartered in Singapore remained free, the solitary event might well have called for explanation. But no such experience is narrated. Military service in these places was attended with unfailing regularity by the following results:—

In Sumatra, in the Dutch regiments, year after year for twenty-two years, beri-beri.

In Singapore, in regiment after regiment, throughout the same consecutive twenty-two years, no beri-beri.

This contrast between the Dutch and British troops is of great epidemiological significance, because (1) it relates to Europeans, the conditions of whose lives are well known; (2) the numbers for comparison are large and

the time and area over which the observations have been spread is very extended.

Again, the American Army of occupation in the Philippine Islands, from 1901 onwards, was composed as follows: Americans 30,000 men (1902-3), 19,000 (1903-4); coloured troops (2,640 in 1902-3 only), Malays or Filipinos (4,800 each year). All were allowed a flour ration, Filipinos the option of rice or flour. Among the whites, there were some cases of beri-beri, 7 to 11 per 10,000 of strength, which may be readily explained by the preference of certain men for rice, or by the acceptance as beri-beri of one of the conditions which resemble it clinically. That is to say, the Americans so long as they ate no rice were exempt from beri-beri. Amongst the Filipinos (rice-eaters) the disease attacked 124 per 1,000 of strength in 1902-3-4, and in 1904-5 even more.

To the above experiences may be added those of the French in Cochin China and Madagascar; and of the combined European and native forces in the expedition to Pekin. Each of those armies comprised rice-eaters and non-rice-eaters, and in each there was beri-beri, but it was confined entirely to the native troops (rice-eaters). Europeans and others who ate no rice were never attacked.

*Racial Preference explained by difference of Diet.*—Compare now with these experiences of one race in different places the incidence of beri-beri in different races in the same locality. In British Malaya the European civil population shares with the native races all the possible factors of causation of disease; there is between them the difference only of food. The natives are rice-eaters, the Europeans are not; the Europeans with rare exceptions never get beri-beri, the natives suffer severely. The Sikhs, Pathans and Punjabis, of whom there are

some 10,000 in the Straits Settlements and Malay States, whose customary diet is wheat flour, exhibit as a community an immunity from beri-beri as complete as that of Europeans. Of 4,237 hospital patients of this class less than ½ per cent. were cases of beri-beri, and of that small number those affected fed on rice.

The exemption which Europeans and natives of Northern India enjoy, when free, prevails also when they are incarcerated in gaols or asylums, if they are allowed their own food. In Singapore Gaol and Singapore Asylum, the latter severely infected by beri-beri, the disease attacked only rice-eaters; Europeans and Indians who were dieted on flour and bread escaped.

TABLE I.

RACE INCIDENCE AND MORTALITY FROM BERI-BERI IN BRITISH MALAYA.

Of 16,716 CASES of BERI-BERI ADMITTED TO GOVERNMENT HOSPITALS, 16,325, or 97 per cent., were CHINESE; CASES among TAMILS amounted to ½ per cent. In 1891 there were 2,757 admissions for BERI-BERI; all but 2 per cent. were CHINESE, TAMILS NONE. In 1901 there were 8,159 admissions for BERI-BERI, TAMILS ONLY 54.

Twenty-five per cent. of all registered DEATHS among CHINESE are DUE TO BERI-BERI. In 2,423 consecutive registered DEATHS among TAMILS (IMMIGRANTS) FROM 1891 to 1900, ONE ONLY WAS ASCRIBED to BEBI-BERI.

TABLE II

RACE INCIDENCE (*Continued*).

Of 328,936 admissions to THIRTY-ONE DISTRICT HOSPITALS in SEVEN YEARS, CHINESE CONTRIBUTED 73 per cent. OF ALL CASES, AND ALL BUT 1 per cent. of admissions for BERI-BERI. Of 79,871 TAMILS ADMITTED, BERI-BERI IS GIVEN as a DIAGNOSIS in ONLY TWO CASES.

Elsewhere also facts conform with those statistics. In Japan, where the disease is endemic among the natives (rice-eaters), the numerous colony of Europeans and Americans and the indigenous Ainhos (non-rice-eaters) escape. It is evident that where beri-beri is endemic those who do not eat rice always escape (see Tables I. and II.).

The converse condition where rice-eaters become attacked by beri-beri in the midst of non-rice-eating communities is illustrated by abundant examples, *e.g.*, the notorious epidemics in New Caledonia which carried off 700 Annamite immigrants in 1891, 600 Japanese in 1892, and 1,000 in 1901. All over the world, in Calcutta, in Australia, in Vancouver, and on the Congo, beri-beri has attacked Japanese and Chinese wherever they have settled, when no factor was peculiar to them save only that their food was rice.

*Special Qualities of Rice essential to the Production of Beri-beri.*—The propositions that beri-beri depends on rice, that it effects rice-eaters only, and that those who eat no rice escape, the writer submits are proved by the general epidemiological evidence. It is, however, sometimes urged that if beri-beri is due to rice its incidence on rice-eaters ought to be everywhere the same, instead of showing violent contrasts as at present, one rice-eating community being unaffected while another is almost exterminated. That argument assumes rice to be always in the same condition, which it certainly is not, and the following facts prove my second contention, viz., that beri-beri attacks only eaters *of certain sorts of rice*.

*Immunity of Tamils to Beri-beri.*—Tamils, natives of Southern India, migrate in thousands yearly to Malaya, and many of them settle there on the expiration of their indentured terms. During the last two decades at least half a million Tamil coolies have lived in British Malaya for periods of over a year, and their numbers to-day may be estimated at 150,000. Within that period still greater numbers of Chinese have been pouring into the same districts, and they now number nearly 600,000. In conditions of toil, fatigue, exposure, influence of climate and place, in deficient sanitation, and depraved habits,

there is no single condition affecting the Chinese to which the Tamil is not equally exposed. The food of the two races, however, differs. For each the staple is rice, but for the Tamil the rice is prepared from grain which is boiled before the husk is removed (cured rice). The Chinese, on the other hand, never use cured rice. Both races, as has been seen, are susceptible to beri-beri. All Tamils as well as Chinese are certified free from beri-beri before landing, and there are thus introduced into a beri-beric area two communities of susceptible individuals, both equally exposed to disease influences, save in so far that there is a distinction in the preparation of their rice.

Although, in ordinary circumstances both communities should equally incur or equally resist beri-beri, the result is far otherwise. Always and everywhere the uncured rice-eating community (the Chinese) suffers from beri-beri; the cured rice-eaters (the Tamils) invariably escape. Thus, of 16,716 cases of beri-beri admitted to Government hospitals, 16,325 (97½ per cent.) were Chinese. The cases among Tamils, including the occasional uncured rice-eaters, amounted to only ½ per cent. In 1891 there were 2,757 admissions for beri-beri, all but 2 per cent. Chinese: the records show no Tamils. In 1901 there were 8,159 admissions for beri-beri. The Tamil proportion should have been 1,119 cases, but the records show only 54, including cases in uncured rice-eaters.

Beri-beri accounts annually on an average for one-fourth of all registered deaths among Chinese, but in 2,423 consecutive registered deaths among Tamils in 1891-1900, one only, and this probably erroneously, was ascribed to beri-beri. In 1907, in 6,239 deaths among Tamils, ninety-seven only were ascribed to beri-beri.

From 1891-1900 the writer had under his care 7,884

Chinese, 43 per cent. of whom had beri-beri, and 3,368 Tamils, of whom only sixteen, or 4 per 1,000, suffered from the disease. Of these latter six were uncured rice-eaters. Apart from beri-beri, Tamils are far more sickly than Chinese.

The exceptions, 5 per 1,000 of all Tamils treated, is less than the proportion which in the British Isles would be admitted to hospitals from various causes simulating beri-beri. To this class belong the cases reported as beri-beri in Tamils, subsisting on cured rice. The statistics, moreover, deal with all cases of beri-beri seen in Tamils, some of whom were known to eat uncured rice, and these figures also include Singalese who do not use cured rice.

Again, during the last three decades there has been in British Malaya a population averaging some 600,000 (Chinese and Tamils). Of these 500,000 were eaters of uncured rice, and 100,000 of cured rice. Among the uncured rice-eaters 80 per 1,000 were attacked annually by beri-beri. Among the eaters of cured rice none were affected.

*Exemption of Tamils is due to their Diet of Cured Rice.*—The figures show that the cured rice-eater is exempt while the uncured rice-eater is attacked, but they do not show that the consumption of cured rice is the only factor peculiar to the Tamil.

Some other condition such as race might, it is suggested, operate to protect the Tamil from beri-beri. Further, the circumstance that, when fed on uncured rice, he gets beri-beri in the same way as the Chinaman, may be met with the supposition that deprivation of cured rice involves loss of other protective factors.

The following two experiments meet these objections:—

(*a*) *Fletcher's Asylum Experiment.* — From the Selangor Lunatic Asylum in which beri-beri was constantly prevalent, all the inmates who had signs of beri-beri were removed, and the remainder in December, 1905, were divided into two parties, one of which was fed on *cured rice*, the other on uncured rice; all subsequent admissions were allotted to one or other of these two parties alternately. Save in their rice, the rations of all were the same; all associated freely, and to test the possibility of place infection (bed bugs, &c.), the parties occupied each others' quarters for alternate terms.

*Results.*—Up to the end of 1906 among 120 patients on uncured rice there were forty-three cases of beri-beri, two of whom were admitted with the disease, with eighteen deaths. Among 123 patients on cured rice there were only two cases of beri-beri both of whom were admitted with the disease. Ten lunatics actually suffering from beri-beri were put on cured rice, and all recovered without relapse; of twenty-six beri-beri patients who were not put on cured rice eighteen died.

On January 1, 1908, after two years on uncured rice, during which beri-beri attacked so many of its members, the first party was put on cured rice, and, since that date (ten months), no cases have occurred. The cured-rice party which for twenty-five months had had no case of beri beri was on the same date put on uncured rice and, in six months, eight cases of beri-beri developed. Since June, 1908, both parties have been on cured rice and both have remained free from beri-beri.

It should be noted that 85 per cent. of the inmates of the Asylum were Chinese, and 10 per cent. Tamils. The immunity of the Tamil cured rice-eater is therefore not racial.

(*b*) *The Durian Tikus Investigation.*—In 1907 the

writer was granted an opportunity by the Government to test by means of this experiment his views as to the cause of beri-beri and the means of preventing it, and the Director of the Institute of Medical Research, Kuala Lumpor, Dr. H. Fraser, assisted by Dr. A. S. Stanton, undertook control of the proceedings.

The experiment consisted in placing on cured rice for a year one half of a force of 300 Javanese who were working at road making, and dieting the other half with uncured rice for the same time. If beri-beri were observed in either party before the expiry of the period, it was arranged that the dietaries would be reversed for the remainder of the time. Other conditions were exactly the same for both parties. During the six months preceding the experiment, which began on May 12, 1907, all the men had been on cured rice, and in April all were examined and found free from beri-beri.

Briefly stated, the results were that the cured-rice eaters remained free from beri-beri, whilst among the uncured-rice eaters beri-beri was prevalent.

### Fresh Rice is Innocuous.

There is also abundant evidence to show that rice eaters who consume fresh village rice, *e.g.*, agricultural Malays and Dyaks, are exempt from beri-beri, so that, among rice eaters, beri-beri attacks only those who eat certain sorts; cured and fresh rice are innocuous. Now as cured rice consists of the whole grain from which, after boiling, only the husk has been removed, rice itself, *quâ* rice, is not poisonous; and the factor in uncured rice which entails beri-beri must be some quality added to or lacking in the original grain. In uncured rice the fat and proteid content is reduced; moreover, the seed,

divested of its protective envelope, readily decays, and is more easily attacked by decomposition. It is always more or less stale.

Numerous observations prove that lack of fat is certainly not a cause of beri-beri; and although there seemed to be more evidence in favour of the proteid starvation view propounded by Takaki, a survey of the published dietaries of the communities among which beri-beri was severe furnishes evidence that proteid, if deficient, was not so much so that its want could have been productive of disease. No one who has seen vigorous young labourers, massive with muscle and otherwise in perfect nutrition, suddenly stricken down and in a few days killed by beri-beri can readily believe that the condition is produced by any form of starvation.

*Considerable Quantities of Toxin Necessary to Produce Beri-beri.*—The presence of a poison in uncured rice explains all the phenomena of beri-beri. Further, the disease is due to a poison which is present in variable proportion, and its effects are proportionate to the quantity of noxious rice eaten, the length of time during which it forms the food, and the degree to which the consumer becomes accustomed to its effects. In epidemics in which the diet was improved, and the disease thereby apparently checked, there was always, simultaneously with the addition of other foodstuffs, a reduction in the amount of rice.

During the Japanese sanitary naval reform the rice of the crews was reduced by 24 per cent., while in New Caledonia it was decreased by 30 per cent. In the Singapore Gaol during 1885 to 1896, *i.e.*, so long as the rice in the dietary was low (35 per cent.), there was little or no beri-beri, but when the proportion was raised in 1897 to 46 per cent.. and in 1900 to 57 per cent., each

increase was followed by outbreaks of beri-beri. The incidence of the disease varies, therefore, not only with the sort but with the quantity of rice eaten.

*The Toxin a Result of Change in the Grain.*—It is plain, therefore, that the toxic quality is an added effect; either the grain itself becomes altered (as by the formation of poisonous proteins, &c.), or it becomes the seat of growth of agents (*e.g.*, ferments, bacteria, fungi) which produce poisons of their own. Both cured and fresh rice are boiled almost at the same time they are husked—the one for preservation, the other for consumption; uncured rice is boiled and eaten only long after it is husked.

The difference between rice which is toxic and rice which is non-toxic is therefore a question of boiling early or boiling late. A time element is here imported, and it implies a change in uncured rice which would not have occurred had the grain been boiled before it was stripped of its envelopes. There can be little doubt that this change is caused by a living force, but whether it is an enzyme or an epiphyte, who can say?

From an observation that horses fed on unhusked rice became affected with a disease resembling beri-beri one conjectures that the active agent lives in or upon the envelopes of the rice, and is able to invade the grain saprophytically when it is husked. Probably also it is peculiar to rice, as the use of no other cereal has been shown to entail beri-beri.

*Practical Results.*—The evidence now laid before you, it is claimed, has proved the theory of rice infection—a theory which from want of facts Van Dieren was unable to do more than indicate as probable; and it has also demonstrated that the change which renders rice poisonous may be avoided by boiling before husking. In the Straits Settlements several of the medical institu-

tions have substituted cured for uncured rice in their dietaries, with the following results :—

At the Singapore Lunatic Asylum, where formerly beri-beri attacked nearly every inmate, Dr. Ellis reports: "From October 13, 1903, to October 13, 1904, all patients were fed on cured rice, and but one case of beri-beri occurred, and that early in November, 1903. In October, 1904, we returned to the uncured rice, and in December fifteen cases of beri-beri arose, although none occurred amongst the controls on cured rice. Cured rice was again resorted to, and in 1906 the official report states :—

"No cases of beri-beri occurred in the Asylum and two patients admitted with it made rapid recoveries."

In the Singapore Prison cured rice was issued to 70 per cent. of the prisoners from November 1, 1904. The months of November and December had usually furnished most cases of beri-beri; and in these two months in the previous year there had been 118 cases. On the new diet there were only twelve (*see* Table III.).

TABLE III.

NUMBER OF CASES OF BERI-BERI OBSERVED IN THE PRISON, SINGAPORE, DURING THE MONTHS OF NOVEMBER AND DECEMBER.

| 1898 | 1899 | 1900 | 1901 | 1902 | 1903 | 1904 | 1905 | 1906 | 1907 |
|---|---|---|---|---|---|---|---|---|---|
| 100 | 24 | 61 | 67 | 87 | 118 | 14 | *Nil* | 1 | *Nil* |

During the ensuing seven months three-tenths of the total rice issued continued to be uncured, and fifteen cases occurred as compared with 147 for the same time in the previous year. From August 1, 1905, onwards only cured rice was used and beri-beri disappeared from the prison. Further, the substitution of cured rice not only prevents the development of the disease, but arrests its progress and promotes cure. In Tan Tock Seng's

Hospital, Singapore, to which about 900 cases of beri-beri are admittedly annually, the mortality fell from 35 per cent. to 17·5 per cent. on the adoption of cured rice (*see* Table IV.).

TABLE IV.

ADMISSIONS FOR BERI-BERI AND MORTALITY FOR SEVEN YEARS AT TAN TOCK SENG'S HOSPITAL, SINGAPORE.

| | 1901 | 1902 | 1903 | 1904 | 1905 (Jan. to May) | 1905 (June to Dec.) | 1906 | 1907 |
|---|---|---|---|---|---|---|---|---|
| Admissions .. | 737 | 715 | 968 | 1,125 | 402 | 464 | 812 | 821 |
| Deaths .. .. | 399 | 305 | 395 | 521 | 193 | 86 | 139 | 102 |
| Case mortality % | 54% | 43% | 41% | 46% | 48% | 18% | 17% | 12% |

After the adoption of cured rice in Province Wellesley there was a reduction in the death-rate from 44 per cent. to 15 per cent., and at Malacca it fell from 28 per cent. to 7·35 per cent. In the hospitals under the writer's own charge in Negri Sembilan, cured rice has been in use since 1907, and in the dietary of beri-berics during 1907 bread was substituted for rice (uncured rice was used by all the other hospitals) with the result that in the former hospitals a far lower mortality has been attained (*see* Table V.).

TABLE V.

CASE MORTALITY OF BERI-BERI IN BRITISH MALAYA DURING SEVEN YEARS, PER 1,000 CASES TREATED.

| | 1901 | 1902 | 1903 | 1904 | 1905 | 1906 | 1907 |
|---|---|---|---|---|---|---|---|
| Perak .. .. .. | 155 | 150 | 165 | 258 | 212 | 318 | 384 |
| Selangor .. .. | 150 | 121 | 183 | 156 | 148 | 192 | 198 |
| Straits Settlements .. | 383 | 300 | 330 | 338 | 332 240 | 142 | 101 |
| Negri Sembilan .. | 40 | 91 | 71 | 54 | 43 | 74 | 64 |

This table furnishes sufficient evidence of the remedial value of cured rice, even if no other facts were available.

*Conclusion.*—As some 2,000 cases annually are admitted

to the hospitals of the Straits Settlements the reduced mortality (25 per cent.) from the adoption of cured rice has been the means of saving many lives. The application of similar measures for the protection of the general public is a more difficult but not an insuperable task; and were it demonstrated—say, in England, as it has been in regard to beri-beri in Malaya—that there was a simple and practicable means of prevention, the public would rightly expect the remedy to be enforced.

# NOTES ON BERI-BERI.[1]

By Dr. A. R. WELLINGTON, Sarawak.

*Read April* 16, 1909.

The actual cause of beri-beri is still uncertain. Many of the facts indicate that beri-beri is infectious, others that it is due to food intoxication; in the case of the Kuching Gaol its disappearance was undoubtedly due to change of diet. It is not proved in Sarawak that *bed-bugs* are carriers of beri-beri, but since the bed-bugs in the General Hospital at Kuching were got rid of no fresh cases have arisen there.

As regards *lice* there is also no evidence except that beri-beri breaks out in gaols and institutions where the inmates are carefully inspected.

With regard to the *rice* theory of infection, beri-beri is unknown amongst the Dyaks, the natives of the interior, who husk their own padi; yet these people if they come to an *endemic area* are just as apt to suffer as the Chinese. That freshly husked rice is not infectious is supported by the case of the Simanggang Gaol, in which the prisoners are fed on native newly husked rice and among whom no case of beri-beri has ever occurred; in Baram, too, it is claimed that the disease has been ousted by feeding people on fresh rice, not necessarily native rice, but *Siam rice*, which looks fresh. On the other hand, among the coolies at Brooketon coal mines beri-beri was at one time rampant, whereas now there is none; yet no change has been made in the rice used, and so, too, at Poak Estate and Bidi mines.

The following instances are cases of apparent infection.

[1] Necessarily abbreviated from the paper sent by Dr. Wellington.

(1) Five Dyaks from a village where beri-beri is unknown came to Kuching in search of work; they remained for five days in Kuching in a Chinese lodging-house, whence they went direct to an estate; they built their house at the edge of the jungle about a mile distant from the rice shop. Here they worked at felling jungle. Within a month all were down with beri-beri and were sent to the General Hospital, Kuching, where one died. The others recovered after a prolonged stay. Their rice was No. 2 Siam, the same as was eaten by the Javanese and other Dyaks on the estate, none of whom had beri-beri. In this instance all five inmates were attacked in one house, and it a new one. These Dyaks probably acquired the disease in the lodging-house at Kuching, which was found to be insanitary, infested with bed-bugs, and used from time to time by those suffering from beri-beri.

(2) Domingo de Rosario, head clerk to the Government Station at Kapit in the Dyak country, where beri-beri is unknown, visited Kuching and lodged in a house where two Chinamen were suffering from beri-beri. Five months later, on his return to Kapit, where only in seasons of scarcity is Siam rice used, he developed beri-beri. Two sons went to nurse him and after his recovery they went to different parts of the country, one of them to a district where only sago is eaten; within a few months both developed beri-beri.

There are many difficulties in tracing beri-beri to rice intoxication; the following are instances:—

(1) Matang Estate was originally worked by Singeh Dyaks, Skrang Dyaks, and Malays: the former alone ate their own rice, the others No 2 Siam. The Singeh Dyaks had no beri-beri, the Malays had very little, the Skrang Dyaks much beri-beri. Some few years later Tamil

labour was introduced, and there were at work 100 Samlas Dyaks, a few Singeh Dyaks and fifty Tamils, all living under the same conditions and eating the same rice (No. 2 Siam). The Dyaks suffered severely from beri-beri, the Tamils had no cases. Still later the Dyak labour was got rid of and Tamils alone have been employed since. In an average daily of 240 (Tamil population) the percentage of beri-beri cases was now 3 per cent. per annum.

Parboiled or cured rice was unknown in Sarawak, and the only difference in the treatment of the rice was that Tamils sift and wash the rice several times before cooking.

(2) In making the Matang Water Works, 1905 to 1908, under exceptionally trying circumstances, Tamils, Javanese, Malays and Chinese were employed, the daily average of these nationalities employed being for the three years: Tamils 131, Chinese 68, Javanese 48, Malays 42. All ate No. 2 Siam rice bought in Kuching, yet there was little or no beri-beri among them, only six cases among the Javanese, three among Tamils, two among Chinese—eleven cases in all in three years.

(3) The Sarawak Rangers, a force comprising Malays, Dyaks, Javanese, Philippines and Sepoys, were housed in large and airy barracks on the top of a hill opposite the town of Kuching. They purchased their rice (No. 2 Siam), which was of the same quality as that used by the general public, in Kuching.

| | | | Non-rice eaters | | Beri-beri | |
|---|---|---|---|---|---|---|
| | | | | | Cases | Per cent. |
| In 1905 this force numbered | 288, | of whom | 76 | were Sepoys | 2* | ·94 |
| ,, 1906 ,, ,, | 320 | ,, | 80 | ,, | 3 | 1·25 |
| ,, 1907 ,, ,, | 340 | ,, | 79 | ,, | 3 | 1·14 |
| ,, 1908 ,, ,, | 328 | ,, | 64 | ,, | 1 | ·37 |

* One of these cases was a Sepoy who was stated to have eaten no rice.

(4) Again, at Bau, a gold-mining centre, where some 1,200 Chinese were engaged in the mines, where there

was great overcrowding, and where the sanitary arrangements were defective, there was very little beri-beri; yet the rice eaten was chiefly No. 2 Siam.

The number of cases stated to have occurred at this centre are as follows:—

In 1905, 5 cases of beri-beri.
„ 1906, 2 „ „
„ 1907, 5 „ „
„ 1908, 6 „ „

So too at Paku, a district with some 6,000 inhabitants, comprising Chinese, Malays and Dyaks, 30 miles from Kuching, where the chief occupation is pepper planting; the Chinese and Malays use No. 2 Siam rice (the Dyaks grow their own), yet beri-beri is even less common than at Bau. The writer estimates the cases at not over twenty per year during 1905-1908, *i.e.*, 3·3 per 1,000.

On the other hand, at Sadong, a coal-mining centre some six hours' steaming from Kuching, beri-beri was rife. The mines are on high ground, the miners chiefly Chinese; the coolie lines consist of long houses divided into compartments; they are planked and raised several feet above the ground, are inspected frequently and kept as clean as is possible. There is overcrowding, but the cubic space is double that of the coolies at Bau. The rice generally eaten is No. 2 Siam imported from Kuching. I examined ten samples taken from rice offered for sale and found them to be, macroscopically, fresh and good.

| | Daily average at mines | Cases of beri-beri | |
|---|---|---|---|
| During 1904 .. | 712 .. | 224 | No change had been made in the rice. None of the Dyaks who lived in the district and had eaten their own rice were attacked. |
| „ 1905 .. | 780 .. | 110 | |
| „ 1906 .. | 656 .. | 69 | |
| „ 1907 .. | 696 .. | 50 | |
| „ 1908 .. | 600 .. | — | |

As possible instances of *place infection*, or of infection conveyed from one individual to another, the following cases may be cited:—

*Paku Gaol*, an old wooden building in which, while beri-beri is rare amongst those in the district (3·3 per 1,000), it is very prevalent among prisoners. The rice eaten by all is the same.

The figures are as follows:—

| | Daily average of prisoners | Cases of beri-beri |
|---|---|---|
| During 1905 .. .. | 25·6 .. .. | 10 |
| ,, 1906 .. .. | 28·9 .. .. | 16 |
| ,, 1907 .. .. | 28·9 .. .. | 5 |
| ,, 1908 .. .. | 26 .. .. | 11 to end of August. |

In *Bau Gaol*, too, beri-beri is prevalent, though comparatively rare in the district (3·75 per 1,000), and the history of an outbreak in this gaol is of considerable interest.

| | | | | | |
|---|---|---|---|---|---|
| The daily average of prisoners during | 1905, | 1906, | 1907, | 1908 to June |
| was respectively .. .. .. | 24, | 32·5, | 18·9, | 19 | |
| and the cases of beri-beri .. | 7, | 49 | 3, | 1 | to June. |

In 1906, with a view to stopping the disease, No. 1 Siam rice was substituted for No. 2, but without result.

On December 11th the Resident arranged for a daily supply of newly husked rice, and this was continued till April, 1908. In the earlier part of the year cases of beri-beri occurring in the gaol were only treated there for a fortnight and were then sent to Kuching, while in the latter part of the year they were sent away as soon as the slightest symptom of the disease showed itself.

Whatever the cause—isolation or change of diet—the disease disappeared and there were but four cases during the next nineteen months.

| Year | Jan. | Feb. | Mar. | Apr. | May | June | July | Aug. | Sep. | Oct. | Nov. | Dec. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1905 | 3 | 1 | .. | 2 | 1 | 1 | 1 | .. | .. | 3 | 2 | 3 | = 17 |
| 1906 | 3 | 1 | 5 | 1 | 6 | 8 | 2 | 3 | 7 | 8 | 5 | .. | = 49 |
| 1907 | .. | 2 | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | = 3 |
| 1908 | .. | .. | 1 | .. | .. | .. | 7 | 5 | ? | ? | ? | ? | |

In the middle of April, 1908, No. 1 Siam rice was resumed, and in July seven cases occurred, in August five cases.

The writer investigated this outbreak and ascertained that the first case was admitted with the disease and had been allowed to remain in the gaol for a month, associating and sleeping with the other prisoners. Here, then, is an instance of beri-beri having been stamped out either by isolation or by change of diet, and of its return when both precautions were relaxed.

Infection may be inferred to be the more important factor because of the rarity of beri-beri among the general population eating the same rice as the prisoners.

Another undoubted instance of the disappearance of beri-beri following the use of freshly husked rice is noteworthy.

Kuching Gaol is situated on the river bank and has an excellent water supply; beyond the fact that there are bed-bugs, it is scrupulously clean. In 1903 110 prisoners contracted beri-beri, the average daily number being 118. During 1902 and 1903 the rice eaten was Rangoon rice. In the middle of May, 1904, newly husked native rice was substituted for Rangoon rice, and is still continued. No other change was made in the dietary.

In the month following its introduction fourteen new cases occurred, being one in excess of any previous month that year; but during the following six months only one case occurred. The total number of cases for the year was fifty-seven, and all but one contracted the disease whilst using the old rice. Isolation was *not* a factor in the decline of this outbreak.

In 50 per cent. of all cases of beri-beri there is a period of invasion, averaging three days, during which there is fever, sometimes so slight as to be overlooked, in other cases fairly severe and akin to influenza. The fever is followed on the third or fourth day by numbness and weakness, and definite symptoms of beri-beri soon appear.

## Discussion.

Dr. Carnegie Brown said that Dr. Braddon's paper was an important contribution to the literature of beri-beri, and everyone in the room, even if unconvinced, must have listened with very great interest to his views, and those of Dr. Wellington on the etiology of the disease. The theory that beri-beri was caused by the development of a fungus, or by a fermentation, or by some other change in rice, and that the symptoms were, therefore, in reality those of an intoxication akin to ergotism, vetch poisoning, pellagra, &c., was not new. It had been put forward many times, and this aspect of the subject had been investigated with special care in Japan, with the result that the theory had been rejected on the grounds that no alteration could be detected in the suspected rice, and that the hypothesis was not in accord with clinical facts.

These conclusions, however, went too far. Beri-beri, it was true, had been eradicated from the Japanese Navy by general sanitary measures, and by the addition of considerable quantities of animal food to a diet which was formerly almost exclusively composed of rice. There had been no special treatment or preparation of the rice ration—which was still issued—but, as Braddon showed, the amount consumed by the men had been very much decreased; and it was reasonably argued by him that the cumulative effect of the toxins might thereby be diminished and counteracted.

At present the position, briefly, was this: The first objection still stood. No organism could be demonstrated in the rice, or in the body of the patient, but that was not necessarily fatal to the theory; the experiences of the Japanese Navy were inconclusive, and the questions of etiological moment at present were:—How far

feeding experiments, such as those of Holst and Fröhlich in Norway, of Eykman and Grijus in Java, and especially those of Travers, Fletcher, Stanton, Braddon, and other investigators in Malaya, gave reliable results, and how far the theory of infection conformed to the epidemiology of the disease? Here, it must be confessed, the difficulties were greater—perhaps insuperable. They were: First, that a disease clinically indistinguishable from beri-beri was frequently seen in persons of whose diet rice formed no part; and second, that the incriminated rice was the principal food — almost the only food — of large communities who lived in the endemic area, and who were absolutely free from beri-beri.

Dr. Braddon, he thought, had not so far met those objections. There was insufficient time that evening to go fully into the interesting questions of the identity of asylum neuritis, ship beri-beri (and many other epidemics affecting peoples who ate no rice, which had appeared from time to time in different parts of the world) with the beri-beri of the Eastern Tropics, but the evidence supplied by these morbid conditions could not be lightly brushed aside by the simple affirmation that they were not beri-beri. Whatever might have been the nature of outbreaks, such as those which occurred in the Richmond Asylum, Dublin, in 1894-96-97, there could be no doubt that the beri-beri of the Singapore and other tropical lunatic asylums was, clinically and pathologically, the same disease which they saw in the tin mines of the Malay Peninsula. Dr. Braddon was himself willing to recognize the asylum neuritis of Singapore Lunatic Asylum as true beri-beri. No doubt that was wholly justifiable, but it was difficult to see why he refused to admit that the exactly similar disease which appeared in non-rice asylums was beri-beri also. In

endeavouring to establish a theory, it was important to avoid even the appearance of selecting facts which were in favour of it, while rejecting those which were against it.

Again, if the hypothesis of change in husked rice were true in its entirety, was not our own supply condemned? As compared with rice eaten in Singapore, it was more likely to be contaminated. The rice of our nurseries and schoolrooms was husked at Rangoon or Chittagong, and it afterwards lay, sometimes for months, in the rice stores and godowns of these ports, awaiting shipment to England; it was almost invariably sent by sailing ship round the Cape, and was, therefore, at least six months more in the tropics before it reached Europe. There was no such thing as fresh rice at home. Probably Braddon would again argue that it was not consumed here in toxic quantities, but the idea was uncomfortable and unpleasant.

With regard to ship beri-beri, evidence was even stronger. Most tropical physicians would be entirely unable to agree with Professors Nocht of Hamburg and Holst of Christiania that ship beri-beri was actually a form of scurvy. He himself had had a considerable experience of ship beri-beri, and had never found a single indication of scurvy or any of the symptoms—hæmorrhages, spongy gums, swellings, &c. — which Nocht said were so common. Experiments on animals, especially on guinea-pigs and pigeons, such as those recorded by Holst and Fröhlich, were unreliable, as polyneuritis was one of the most common laboratory diseases; and, although the work of Eykman and Grijus in Java was more accurate—and some of that, such as the inhibition of beri-beri by the administration of a watery extract of the padi husks, strongly supported

Braddon's views—it was insufficient to establish a convincing theory of infection. Moreover, the analogy between human beri-beri and experimental neuritis in animals was fallacious, even if the latter could be scientifically and accurately induced. Again, it was very difficult to get over the outstanding fact that in Italian sailing ships, where a considerable quantity of rice was eaten, and where the general conditions were often unfavourable, beri-beri was unknown; while in Norwegian vessels, where the feeding was liberal, and the physique of the crews was much above the average, the disease was extremely prevalent. No rice, it should be noted, was eaten in Norwegian ships, the sailors preferring rye and wheaten bread.

By far the most prominent clinical feature of all those forms of neuritis, and of the beri-beri of the East Indies—and one which closely connected them—was that they were essentially diseases of association. When men had to live together, as in mining camps, agricultural coolie lines, asylums, hospitals, gaols, ships, and fishing stations, beri-beri, in the Eastern Tropics, was almost inevitable; and the greater the crowding together the greater was the liability to the disease. When family life was possible, when the labourers could have their own huts and gardens, and live, as men were intended to live, with their wives and children under their own roof-tree, beri-beri was never heard of. And this immunity existed although the sanitary conditions were often deplorable, although they were in the centre of the endemic area, and although they lived almost exclusively on uncured rice. They were exposed to the same sun, did the same work, drank the same water, and ate the same food, but still they remained free from the disease, while their comrades in the Kongsi

houses furnished a heavy toll to its ravages. In the districts and the towns with which Dr. Braddon dealt there were thousands of Chinese households, who lived all their lives on the rice which was said to engender beri-beri, and yet, so long as home life continued, not one member of the family was ever attacked by the disease. On the other hand, if a man from one of those houses went to work in a mine, where he messed and lived in association with many others, or if he had the misfortune to get into gaol, or an asylum or hospital, he was extremely likely to acquire beri-beri.

Probably, in the production of the disease there were more causes than one, but these feeding experiments recorded by Dr. Braddon were certainly very striking. His theory, indeed, had now passed beyond the range of experiment, and entered that of legitimate treatment, so that the last difficulty in testing it thoroughly had disappeared. By its results as a practical method it would fall or stand. The case, clearly as it had been argued, was not yet, however, complete. Although it was now difficult to deny the possibility of contaminated rice being a factor in causation, until the clinical anomalies which he had instanced were explained, it could only be regarded as a factor. General experience still pointed to the conclusion that rice alone, cured or uncured, could not induce the disease, and that other conditions besides those of diet were essential.

Colonel LEISHMAN said that his knowledge of beri-beri was more or less limited to the literature on the subject; he had had very little practical experience. The question seemed to be surrounded by very great doubt, every paper (as was the case with those the Fellows had heard that evening) sounding more convincing than the

previous one. Thus, after listening to Baron Takaki, when he propounded the theory of nitrogen starvation, he (Colonel Leishman) left the lecture room with a strong feeling that the difficulties of the subject had at last been cleared away. Again, there were theories of protozoal infection, a coccus and other bacilli had been isolated, and these in turn seemed to make it very certain that the story of beri-beri was perfectly definite and simple. To-night they had heard in the first paper a strong and powerful argument in favour of rice causation; but the paper that followed threw considerable doubt on that theory, for he gathered that the views of Dr. Wellington did not coincide with Dr. Braddon's theory. The Honorary Secretary had given a clear summary of our present knowledge of the disease, and he thought perhaps beri-beri might now be connected in some way with the eating of rice. Certainly some of the epidemiological facts with regard to rice-eaters were too strong to be swept aside. Personally, he confessed, he favoured the theory of protozoal infection, which might, as has been suggested, act as the causative agent in the form of a parasite of the weevil.

Dr. James Maxwell (Formosa) alluded to the question of storage of rice. The Hon. Secretary had referred to the prevalence of beri-beri in Institutions, and the absence of that disease amongst people living in the country. He (Dr. Maxwell) did not know the practice in the Straits, but, in Formosa, rice was stored unhusked, and it was husked only when required for immediate use; and in the country districts beri-beri was seldom or never seen. In cities, on the other hand, rice was very frequently husked first and afterwards stored: and, in those circumstances, it had occurred to him that beri-

beri was more common than was the case where rice was used immediately after husking.

Dr. CARNEGIE BROWN said, in reply to Dr. Maxwell, that rice grown in Malaya was insufficient for the supply there, but that it was generally husked in the Straits, and might be regarded as fresh. On the other hand, the rice which was mostly consumed was grown and husked in Burmah or Siam and then stored in bags for quite long periods—very often for five, six, seven or eight months. The method of storing the rice did not, however, seem to him to play an important part in producing beri-beri. As an illustration he instanced the case of an institution in Malaya where there were a large number of natives of Eastern Asia who were being trained as missionaries by a staff of exceptionally capable European priests. There were in this institution many young men, most of whom had been there several years. They had plenty of exercise; their diet contained considerable quantities of meat, and they had in general the best of health. This institution was situated in the midst of a large population of native Christians—principally Chinese and Portuguese, dwelling in their houses and eating rice from the same source as the inmates of the institution. Naturally it was their principal food, and both were on equal terms in that respect, but in the College the diet was perhaps a little better than in the district. The rice, which came from rice mills in Rangoon, he found was husked as a rule three or four months before it was consumed, and was then stored in the local rice shops. In the district there had been no case of beri-beri, but in the institution—where the conditions were altogether much better—there had unfortunately been several instances of the disease.

Mr. CANTLIE said the question of the storage of rice was of much interest, and he would refer the Fellows to an article published in the *Journal of Tropical Medicine* some six years ago on that subject. The writer conducted operations in the Pearl Fishery off the West Coast of Australia; he engaged a small fleet of ships, which he manned by Japanese, and these Japanese sailors and divers on every expedition which was undertaken developed beri-beri after a period of about seven months—never before. In these expeditions the rice was shipped at the commencement of the voyage and stored on board. The men kept perfectly well until a definite time—the seventh month—when the disease manifested itself. So regular was the period of occurrence, and so well known were the symptoms, that the expeditions were ordered to return to port before the seventh month. If the return was delayed beyond this period beri-beri invariably broke out. It looked, therefore, as if long storage of rice had something to do with the occurrence of the disease. He thought, however, they might easily attach too much importance to diet. For instance, there was no leprosy in the north of China and much leprosy in the south of China; in both these parts of the country rice was eaten. But it would be unwise to consider anything was proved by that fact. It was necessary to weigh the facts very carefully before associating a disease such as beri-beri with any particular diet. He recalled instances to which he had previously drawn attention, of patients with open wounds having contracted beri-beri, while patients in the same ward whose skin was uninjured escaped the disease. Thus, again it would appear, if anything could be concluded from these cases, that diet had nothing to do with the question.

Dr. Low said he would not add to the controversy

as to the etiology of tropical beri-beri, but, as regards ship beri-beri, he thought one of Dr. Braddon's weakest points was in maintaining that it was not true beri-beri. He had seen cases of ship beri-beri in Norwegians in Barbados, and in Chinese, Lascars, and other natives from ships that came to the docks in this country; and, so far as he could make out, the disease was identical with that seen in the East. The patients had all the symptoms of beri-beri and no evidence of scurvy. They had no spongy gums, no hæmorrhages, nor any of the other typical signs of scurvy. Cases of neuritis, however, might possibly be due to different causes, especially those which came from the mines in the East. On the whole, after having read Dr. Braddon's book it seemed fairly clear that uncured rice was presumably a causative agent; but it should not be overlooked that Dr. Wellington also had investigated a large number of cases, and his conclusions seemed to be diametrically opposed to Dr. Braddon's. One point in particular that impressed him (Dr. Low) was the statement by Dr. Braddon that so many hundred coolies ate one sort of rice only. Evasion of dietetic rules was difficult to repress, and although as a body this might apply, he thought it would be very difficult to state this as a fact with regard to each individual.

Dr. KERR said that he would like to add one fact to the debate. Since the inmates of the institutions of the Straits Settlements—not the Federated Malay States—had been fed on cured rice, no case of beri-beri had occurred in them.

Dr. BRADLEY, of the Seychelles Islands, said that, when he went there, beri-beri was unknown. The population was about 4,700, and they ate rice, fish, &c., but until recently he had never seen a case of beri-beri.

St. Pierre, an island about 200 miles off the mainland, had, however, lately been opened up by an English Chemical Company. It had no water supply, and the employees had to drink water distilled from sea-water. On commencing this they immediately had an outbreak of beri-beri there. Recently, also, in the prison in the Seychelles, there had been small outbreaks of beri-beri. The food consisted of rice, fish and manioc—practically the same food as that which outside people ate—only it was in reduced quantities. As a rule, the prison was pretty full, but even when fairly empty cases occurred; there were many bugs. The rice was ordinary quality, costing ten or twelve rupees a bag, and it was at least five or six months old. In his opinion beri-beri did not depend upon any one particular thing. It certainly did not depend altogether upon rice, for all prisoners did not eat rice, yet non-rice-eaters did get beri-beri. Even when the diet was changed the prevalence of the disease did not seem to be affected.

Sir PATRICK MANSON suggested that on account of the importance of the subject further discussion be adjourned until next meeting, and said that, although it was very late, he would like to make one or two general observations. When he was asked by the Colonial Government as to the desirability of giving Dr. Braddon an opportunity of proving his views on the subject of beri-beri, he acquiesced, and he was quite sure that unless this opportunity had been given the Society would not have heard of this investigation as to whether rice was one of the causes of the disease.

Unfortunately, in his opinion, although so many facts had been accumulated, nothing conclusive had been proved. Dr. Braddon's theory was still unproved, but

great merit attached to him for having realized the possible significance of the coincidence that the Tamils in the Straits Settlements did not get beri-beri and that they did not eat the ordinary rice consumed by the Chinese. It is just possible that he might be right that this was cause and effect, but it was not yet proved. Dr. Braddon had quoted Fraser and Stanton's recent feeding experiments by cured and uncured rice, but he had omitted one rather important fact which, in his (Sir P. Manson's) opinion, indicated a possible fallacy in his conclusions. Drs. Fraser and Stanton had the opportunity of experimenting with gangs of coolies under exceptionally favourable circumstances, feeding a certain proportion on cured and a certain proportion on uncured rice, with the invariable result that those fed on cured rice got no beri-beri, but a proportion of those fed on uncured rice got beri-beri. In one instance a gang had remained for many months on one particular station feeding on uncured rice, and was free from beri-beri. The month after their removal to another place the men at once began to contract the disease. No change had been made in the food, but there was a change of station. That was an important point, and he mentioned it because he thought the *cons* as well as the *pros* should have been given. As regarded his (Sir Patrick Manson's) own views he preferred to keep an open mind, and until they got the germ or toxin, or whatever it might be, of beri-beri, and could administer it directly to willing subjects, and watch the results, he would not subscribe to any theory. He had recently seen Dr. Hamilton Wright and had asked him what he thought about the rice theory. Dr. Wright said it was not true to Nature. He had heard that the Tamils in Rangoon got beri-beri, although they lived on cured rice. He had visited Rangoon, and he found that the

Tamils there living on Indian rice did get beri-beri. If that were so it upset Dr. Braddon's theory. With reference to the actual process of curing, he (Sir Patrick Manson) had asked Colonel Prain, Director of the Royal Botanic Gardens at Kew, if he could tell him how rice was cured in India, and the Director after enquiry sent him the following reply. As the question of the parboiling of rice was a matter of some interest in connection with beri-beri, he thought it well that this accurate and authentic information should be put on record. The process was as follows :—

Paddy is soaked in cold water for twenty-four to thirty-six hours. It is then removed in a large earthen pot (*handi*) and boiled with a little water (about half a seer in a *handi* containing about ten seers of paddy) until some of the grains burst. The grains are then dried in the sun on a mat. The drying process is thought to be completed when the grains inside the husks become hard. The husks are then removed by a wooden machine called a dheki.

As regarded the difference between ship beri-beri and ordinary land beri-beri, he had seen many cases of both and had failed to recognize any clinical difference. If ship beri-beri were the same as land beri-beri, certainly in every instance rice was not the cause of the disease. The other day he had had two cases in hospital, both from the same Norwegian ship. One of these cases was suffering from the œdematous form of beri-beri, and the other from the paralytic. He asked the patients if they ate any rice, and they said they had about a spoonful once a week. In these cases, therefore, rice was certainly not the cause.

(*Discussion adjourned.*)